Nuclear Spin Relaxation Spectroscopy

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From the time dependence of the nuclear spin relaxation phenomena, molecular structure, conformation, motions, interactions, diffusion, and adsorption can readily be studied. Aside from the studies at the molecular level, nuclear spin relaxation phenomena have been applied to qualitative and quantitative analysis in the areas of polymer research, agriculture and food research, petroleum research, and medical research. This article presents an introduction to the theory, techniques, and applications of nuclear spin spectroscopy.

Index Headings: NMR spectroscopy; Spin-lattice relaxation; Spin-spin relaxation; Theory; Experimental methods; Data reduction; Molecular dynamics; Qualitative and Quantitative analyses.

INTRODUCTION

Nuclear magnetic resonance (NMR) chemical shifts, coupling constants, and areas of resonance lines are some of the most useful and powerful diagnostic parameters measured by the chemist to determine the structure, conformation, and composition of molecular systems. Within the last 5 years the determination of nuclear spin relaxation times has become still another NMR parameter with both practical and theoretical significance.

The phenomenon of NMR relaxation has been studied since 1950, but such studies were largely confined to specialists because of the theoretical complexity and experimental difficulties. With the advent of commercially available pulsed Fourier transform NMR spectrometers, the determination of the relaxation times for each magnetic nucleus within a molecule was greatly simplified. This simplification of the technique has resulted in the use of relaxation time measurements as a probe to investigate the structure and conformation of molecules, molecular motion, molecular interactions, kinetics of molecular systems, adsorption of molecular species, the quantitative analysis of natural and industrial products, and the mechanism of the relaxation phenomenon itself.

Because of the recent upsurge in nuclear relaxation measurements, it has become necessary for the chemist to become familiar with concepts, applications, and instrumentation of the technique. This article contains a general description of the theory, the instrumentation, data processing methods, and some applications of chemical interest. For a more rigorous treatment of the theory, molecular dynamics, applications, and factors affecting relaxation times, the reader is referred to the literature cited in the text.

I. GENERAL DESCRIPTION OF NUCLEAR SPIN RELAXATION

The fundamental property of the nucleus, which allows magnetic resonance to exist, is the nuclear spin angular momentum, \( I \), which is quantized in integer or half-integer values of Planck's constant, \( h \). Associated with the spin, \( I \), is a magnetic moment, \( \mu \), which ultimately gives rise to the observed NMR signals. For \( I = \frac{1}{2} \) in the absence of a magnetic field, the energy levels are degenerate. When a sample is placed in a magnetic field, the degenerate nuclear spin energy states are split as shown in Fig. 1, A and B. The lower energy state for the case \( I = \frac{1}{2} \) contains a greater proportion of the nuclear spins than the upper energy state as prescribed by the Boltzmann distribution function. If a nuclear spin system is perturbed by a short but finite radiofrequency (rf) pulse, there is a redistribution of spins. The upper energy state may become populated to a greater extent than the lower energy state (see Fig. 1C). After the perturbation (Fig. 1D), the spin system must revert to its original equilibrium condition (Fig. 1B). The recovery process by which the spin system returns to the equilibrium state is referred to as relaxation. The relaxation process occurs through the coupling interaction of the nuclear spin moments with resonance frequencies generated by fluctuating local magnetic and electric fields, which in turn are produced by thermal motions of the molecules and the inhomogeneity of the magnet. The extent of the coupling depends upon the magnitude and rate of fluctuation of the local fields. The time dependence of the fluctuating local magnetic fields is related to the molecular dynamics of a molecule in any given physical state.

A. Theory. The NMR signal depends upon the difference in the spin population of the nuclear spin energy states (Fig. 1B). Thus, the rate of change of the NMR signal after a perturbation is related to the rate of change of the spin population between the energy states, which in turn depends upon the relaxation mechanism.

Changes in the population of the nuclear spin states can best be described by a vector representation of the net magnetization of the nuclear spins in a rotating frame coordinate system. Specifically, the coordinate...
Ho, and co is the angular frequency of H1. T~ is the relaxation times are used to characterize the nuclear spin transverse or spin-spin relaxation time. These two re-

perturbation phenomena in solids.~b

magnetic field strength, H1, applied perpendicular to the external magnetic field H0 (Fig. 2A).

When a spin system is perturbed with an rf pulse (of magnetic field strength, H1, applied perpendicular to H0), the magnetization vector M0 is rotated towards the x’y’ plane giving rise to magnetization components Mx’, My’, and Mz’, in the y’ and z’ directions, respectively (Fig. 2B). If the intensity of the pulse, H1, and its duration or pulse width, t~w, are properly chosen, M0 can be rotated away from the z’ direction through any angle, α. For a 90° rotation (π/2) shown in Fig. 2C, the expression for α is

\[
\alpha = \pi/2 = \gamma H_1 t_w
\]

where γ is the gyromagnetic ratio of the nucleus being investigated. In this case the magnetization component Mz’ = 0 and Mx’ = M0. For molecules in the liquid or gaseous state the rate of change of the nuclear magnetization vectors, Mx’, My’, and Mz’, in the x’, y’, and z’ directions after perturbation can be described by three first-order differential equations (Eqs. (2), (3), and (4)). \(1^b\) Provotorov equations are used to describe spin perturbation phenomena in solids.

\[
du/dt = -u/T_2 + (\omega_0 - \omega)v \tag{2}
dv/dt = -v/T_2 + (\omega_0 - \omega)u - \gamma H_1 M_{x'} \tag{3}
dM_{x'}/dt = -(M_{x'} - M_0)/T_1 + \gamma H_1 v \tag{4}
\]

where H1 is the applied rf magnetic field, u is the component of M0 along the direction of H1, and is equal to Mx’ cos ωt – My’ sin ωt, v is the component of M0 perpendicular to the direction of H1 and is given by –Mx’ sin ωt – My’ cos ωt, γ is the gyromagnetic ratio, ω0 is the angular frequency of the external magnetic field H0, and ω is the angular frequency of H1. T1 is the longitudinal or spin-lattice relaxation time and T2 is the transverse or spin-spin relaxation time. These two relaxation times are used to characterize the nuclear spin relaxation process. The spin-lattice relaxation time, T1, governs the return of the z’ magnetization vector to its equilibrium Boltzmann distribution value, M0, after a perturbation, and the spin-spin relaxation time, T2, governs the return of the x’ and y’ magnetization vectors to their equilibrium value of zero. The spin-lattice relaxation time has also been defined as the average lifetime of the nuclear spin in the excited or higher energy state and the time necessary for the spins to come to equilibrium with the lattice. The term “lattice” represents the translational and rotational degrees of freedom of the molecular system. Vibrational degrees of freedom are too fast on an NMR time scale to provide a mechanism for relaxation.\(^2\) A very long T1, or T2 indicates an inefficient relaxation process.

The spin-spin relaxation process is an adiabatic exchange of energy among the spins; that is, the total energy of the process is conserved and is not transferred to other parts of the system. After a strong perturbation of the nuclear spin system, the nuclear moments of the nuclei are in phase with each other and have a net magnetization component in the y’ direction within the x’y’ plane (Fig. 2C). After termination of the pulse, spin-spin interactions cause the nuclear moments of the precessing nuclei to get out of phase with one another. Thus, some moments rotate faster and some slower than the rotating reference frame, resulting in a loss of phase coherence or a “fanning out” of the individual nuclear moments (Fig. 2D). After a certain amount of time the nuclear moments are again equally distributed about the axes of the external magnetic field, resulting in a zero y’ magnetization component. The lifetime for this loss of phase coherence is the spin-spin relaxation time, T2.

Loss of phase coherence can also result from inhomogeneity in H0. Thus the observed spin-spin relaxation rate (1/T2*) (Eq. (5)) is the sum of the inherent relaxation rate for the sample (1/T2) and the rate due to magnetic field inhomogeneity (1/T2’)

\[
R_2^* = 1/T_2^* = 1/T_2 + 1/T_2' \tag{5}
\]

Both spin-lattice and spin-spin relaxation processes are affected by high frequency fluctuations from local magnetic fields that result from molecular motion, whereas low frequency fluctuations affect only spin-spin relaxation processes. Mechanisms resulting from fluctuating magnetic fields are discussed in the next section.

B. Relaxation Mechanisms. Dominant mechanisms for spin-lattice and spin-spin relaxation processes for a nucleus can arise from five sources of fluctuating local magnetic fields: (1) dipole-dipole interaction with other

![Fig. 2. The effects of an intense rf pulse on the macroscopic magnetization vector, M0, in a rotating frame coordinate system. A, at equilibrium M0 is colinear with H0; B, during a pulse M0 rotates about the x” axis; C, rotation of the magnetization vector with a 90° pulse; D, after the pulse with loss of phase coherence in a homogeneous field.](https://example.com/figure2.png)
magnetic nuclei or with unpaired electrons from dissolved oxygen or paramagnetic sources; (2) spin-rotation interactions involving quantum-rotational states of the molecule or group; (3) electric quadrupole interaction resulting from coupling of a nuclear spin for nuclei having spin \( >\frac{1}{2} \) with the electric field gradient at the nucleus; (4) scalar interaction arising from a chemical exchange process or with a nucleus undergoing rapid relaxation because of quadrupolar relaxation; and (5) chemical shift anisotropy interaction resulting from the tumbling of molecules that have directionality of the magnetic shielding about the nucleus. Conduction electrons and excited "excitons" can also provide a relaxation pathway. These mechanisms are only encountered in very specific types of material.

Not all of the mechanisms operate for any given nucleus at the same time. The predominant mechanism will depend on the nuclear spin and on the size, symmetry, physical state, and temperature of the molecule. Also, it is not necessary that the predominant mechanism for \( T_1 \) be the same for \( T_2 \).

The relaxation times for the various mechanisms can be derived from time-dependent perturbation theory.\(^4\) Different theoretical approaches are given in the papers by Bloembergen et al.,\(^5\) by Kubo and Tomita,\(^6\) and by Redfield.\(^7\) Reviews and standard texts devoted to the subject of nuclear magnetic relaxation are also available.\(^8\)-\(^11\)

In the following discussion on each of the relaxation mechanisms, emphasis has been placed on the spin-lattice relaxation process. The techniques for obtaining \( T_1 \) values are generally easier than those for \( T_2 \) measurements, and thus most molecular systems investigated have been interpreted in terms of spin-lattice relaxation times. Equations for \( T_2 \) differ only slightly from those to be listed for \( T_1 \). The interested reader is referred to the text by Abragam.\(^4\)

1. Dipolar Relaxation Mechanism. The dipolar contribution to the spin-lattice relaxation time can be divided into three interactions: (1) the direct bonding intramolecular interaction, (2) the intermolecular interaction, and (3) the long-range intramolecular interaction of nuclei. The largest contribution to the dipolar spin-lattice relaxation time is that of the directly bonded nuclei. In general, the relaxation time of a nucleus with spin, \( S \), is inversely proportional to the number of attached nuclei with spin, \( I \), and directly proportional to a sixth power of the internuclear distance. Intermolecular interaction effects arising from hydrogen bonding, complexation, solvation, metallic paramagnetic sources, and oxygen can also contribute significantly to the dipolar relaxation time. The contribution to the dipolar spin-lattice time due to long-range intramolecular interactions is the least significant of the dipolar relaxation mechanisms.

The theoretical expression for the intramolecular dipolar spin-lattice relaxation time for a system of two different spins, \( I \), and \( S \), is given as follows:\(^8\)

\[
1/T_1^{DD} = \frac{2\gamma_I^2\gamma_S^2I(I+1)h^2}{15\tau_{c}^2} \left[ \frac{\tau_c}{1 + (\omega_1 - \omega_S)^2 \tau_c^2} \right] + \frac{3\tau_c}{1 + \omega_S^2 \tau_c^2} + \frac{6\tau_c}{1 + (\omega_1 + \omega_S)^2 \tau_c^2} \tag{6}
\]

where \( \gamma_I \) and \( \gamma_S \) are the gyromagnetic ratios for nuclei with spins \( I \) and \( S \), respectively; \( h \) is Planck’s constant divided by \( 2\pi \); \( \tau_{c}^2 \) is the internuclear distance between nuclei with spins \( I \) and \( S \); \( \omega_0 \) is the frequency of the nucleus being observed; \( \omega_I \) is the frequency of the attached nucleus; and \( \tau_c \) is the molecular rotational correlation time.

A physical description of the motions of a molecule is contained in the molecular rotation correlation time, which is defined as the time necessary for the molecule to reorient one radian. Thus, the correlation time depends on the size and symmetry of the molecule, intermolecular interactions, the viscosity, and the temperature all of which affect the observed spin-lattice relaxation rate. A plot to \( T_1^{DD} \) vs \( \tau_c \) at various field strengths is shown in Fig. 3.

The dipolar spin-lattice relaxation time decreases with increasing \( \tau_c \) until a minimum is reached. To the left of the minimum in Fig. 3 the product of the frequency and \( \tau_c \) terms in Eq. (6) is much less than 1 and Eq. (6) reduces to

\[
1/T_1^{DD} = (4/3)\gamma_I^2\gamma_S^2h^2(I+1)\tau_c \tag{7}
\]

This particular situation is referred to as the "motional or extreme narrowing condition" and is generally applicable to small molecules in the liquid state. For \( N \) magnetic nuclei with spin, \( I \), bonded to nucleus with spin, \( S \), the relaxation rate is the sum of each \( I-S \) interaction.

\[
1/T_1^{DD} = \sum_N (4/3r_0^6)\gamma_I^2\gamma_S^2h^2(I+1)\tau_c \tag{8}
\]

As the temperature increases and the viscosity decreases for a molecular system, \( \tau_c \) gets shorter and the spin-lattice relaxation time increases. Molecular systems in which \( \tau_c \) is to the right of the minimum in Fig. 3 show the reverse behavior with respect to temperature and viscosity changes. This behavior has been noted for large molecules, for small molecules in viscous solutions, and for solids.

The manner in which temperature and viscosity affect the intramolecular dipolar relaxation rate for an isotropic, rigid molecule can be derived from Eq. (7) assuming the condition of motional narrowing and using a physical model that describes the motion of molecules in solution. Both diffusion\(^12\) and the inertial-controlled\(^13\) models for the reorientation of a molecule in

**Fig. 3.** Dipolar spin-lattice and spin-spin relaxation times as a function of the molecular rotational correlation times at various magnetic fields.
solution have been used. Both models are based on the assumption of spherical molecules and do not account for motional anisotropy arising from nonspherical molecules with large differences of the moment of inertia about the principal axes of the molecule or the preferred direction of diffusion. Anisotropic reorientation of molecules in solution has been considered. Woessner considered ellipsoidal molecules undergoing anisotropic rotational diffusion and calculated the dipolar spin-lattice relaxation rate.

For a small organic molecule within the limits of diffusion control, the $^1$H dipolar relaxation rate, $1/T_1^{1H}$, is given by Eq. (9):

$$1/T_1^{1H} = 1.4 \times 10^{-9} N \gamma^2 \gamma_c^2 \gamma_H^2 (M \eta/T \rho) r_{CH}^6$$ (9)

Thus, it can be seen that the dipolar relaxation rate is directly proportional to the molecular weight, $M$, and the viscosity, $\eta$, and inversely proportional to the temperature, $T$, and the density, $\rho$, of the molecular system.

To a first approximation Eq. (9) has been used by Lambert and Netzel to rationalize the observed spin-lattice relaxation times for saturated heterocycles. It was assumed that the viscosities and densities of the saturated heterocycles investigated are similar and that at a constant temperature of 303°K the major contribution to the spin-lattice relaxation is dipolar. A plot of the observed relaxation rate vs the molecular weight of the pentamethylene heterocycles was found to be linear, as shown in Fig. 4 for the $\alpha$-carbons of these heterocycles of groups IV, V, and VI.

Fig. 4 shows that there is an apparent correlation of the observed spin-lattice relaxation rate with the molecular weight. Piperidine does not correlate nearly so well as the other saturated heterocycles. The shorter relaxation time (an increase in the spin-lattice relaxation rate) was attributed to the increase in the molecular orientation correlation time as the result of an increase in the size of the molecular species due to intermolecular hydrogen bonding.

Theoretical treatment of intermolecular interaction as it affects spin-lattice relaxation times is extremely difficult because it must rely on a theory for liquid mixtures. The intermolecular dipolar spin-lattice relaxation time depends on both the translation and rotational motion of the molecules in solutions. With the use of rather crude assumptions, the intermolecular spin-lattice relaxation rate is given by

$$1/T_1^{1H} \text{(inter)} = (16/45) N \gamma I^2 \gamma_S^2 \gamma_H^2 (I + 1)/a (D_I + D_S)$$ (10)

where $D_I$ and $D_S$ are the self-diffusion constants for molecules containing spins $I$ and $S$, respectively, $a$ is the distance of closest approach between spins $I$ and $S$, and $N_I$ is the concentration of spin $I$.

Qualitative statements based on Eq. (10) can be made as to the important factors affecting intermolecular relaxation times. The most significant difference between the relaxation equations for inter- and intramolecular dipolar interactions is the spin concentration term, $N_I$, for intermolecular dipolar relaxation. The relaxation time is inversely proportional to the concentration of the number of spins and the square of the gyromagnetic ratios. Thus, small concentrations of paramagnetic impurities such as dissolved oxygen, metallic ion, and/or paramagnetic organometallic complexes drastically reduce the relaxation time because of the large gyromagnetic ratio for the unsupported electrons in these types of compounds.

Temperature and viscosity effects can be predicted through the self-diffusion terms for each molecular species. Higher temperatures and lower viscosities will result in longer $T_1^{1H} \text{(inter)}$.

In most applications of spin-lattice relaxation times it is necessary to reduce the intermolecular dipolar interaction contribution to relaxation rate for meaningful interpretation of the data. Thus, samples are degassed to remove oxygen or treated with EDTA to remove metallic ion impurities, and low magnetic or nonmagnetic solvents such as CCl$_4$, CS$_2$, and deuterated compounds are used.

2. Spin-Rotation Relaxation Mechanism. The molecular rotation states of a molecule provide a direct mechanism for nuclear spin relaxation. The coupling interaction for the transfer of nuclear spin energy to the lattice is between the nuclear magnetic moment of the resonating nucleus and the frequencies generated by the fluctuating local magnetic fields that result from the rotational motion of the electron distribution in a molecule. This mechanism is distinct from the molecular reorientation influence on two interacting dipoles in dipolar relaxation and thus has a correlation time that is dependent on the angular momentum associated with the rotating molecule.

In general, the time scale for the spin-rotation mechanism to be effective is too rapid for most molecular systems. The spin-rotational interaction is most effective for small symmetrical molecules and dominates the relaxation mechanism for nuclei of spin $1/2$ in the gas phase, for neat liquids of low molecular weight, for nonpolar solvents at high temperature and low viscosities when unhindered rotation is present, and for non-protonated carbons. Also, the spin rotation mechanism is more prevalent for nuclei with greater nuclear charge than for lower nuclear charge. Thus, the mechanism is more likely to be important for $^3$P, $^3$P, $^3$N, and $^3$C.
than for \(^1\text{H}\). In fact, spin-rotation has been found to be a significant mechanism for \(^{31}\text{P}\) \(^{19}\text{F}\) and \(^{19}\text{F}\) \(^{29}\text{P}\) nuclei in the solid state. Typical values for spin-rotation relaxation times for various nuclei fall in the range of \(10^{-2} \leq T_1 \leq 10^2\) s.

The spin-rotation mechanism is not usually dominant in large molecules. However, if \("f ree\) rotating groups such as \(\text{CF}_3\), \(\text{CH}_3\), \(\text{ONO}\) are part of a large molecule, nuclei in these groups can relax by spin-(internal rotation). From the temperature dependence of the spin-(internal rotation) relaxation time, the barrier to internal rotation can be determined.

The theoretical expression for computing the spin-lattice relaxation time due to spin-rotation interaction is given in Eq. (11):

\[
1/T_{1SR} = 2kT h^{-2} I_m C^2 \tau_{SR}
\]

where \(k\), \(T\), and \(\hbar\) have their usual meaning, \(I_m\) is the moment of inertia, \(C\) is the isotropic spin-rotation interaction constant, and \(\tau_{SR}\) is the spin-rotation correlation time.

The equation has been derived under the assumption that the molecule is spherical, has isotropic motion, and is in the limit of extreme narrowing. Derivation of the spin-rotation relaxation time has been extended to nonspherical molecules and to molecular systems having motional anisotropy. However, the resulting equations are complex since both \(I_m\) and \(C\) are tensor quantities.

Calculating the spin-rotation relaxation time from Eq. (11) is not usually possible since the spin-rotation coupling tensor \(C\) is not known for many molecules. The value of the coupling tensor can be obtained experimentally from molecular beam resonance or very high resolution rotational spectroscopy. The tensor may also be estimated from chemical shift data since both the spin-rotation interaction and the chemical shift depend on the electronic distribution about the nucleus. \(^{13}\text{C}\), \(^{19}\text{F}\), or \(^{31}\text{P}\) are likely to have strong spin-rotation interactions.

The spin-rotational correlation time, \(\tau_{SR}\), is related to the lifetime of a molecule in a given angular momentum state. For gases, where the number of molecular collisions is small relative to liquids, the lifetime of the angular momentum state of a molecule is relatively long. A long lifetime corresponds to a long \(\tau_{SR}\) and thus a short relaxation time. The relaxation time for liquids is long relative to gases because of the many molecular collisions shortening the lifetime of the angular momentum state of the molecules.

The temperature dependence of the spin-rotation relaxation time is mainly due to changes in \(\tau_{SR}\). As the temperature of a molecular system increases, a greater number of molecules reside in the higher rotation energy states. The overall lifetime of the angular momentum state is increased which in turn results in a decrease in the relaxation time. The decrease in the relaxation time as temperature increases is illustrated in the temperature dependence of the spin-(internal rotation) relaxation mechanism for the ONO group (Fig. 5)\(^{21}\) for \(^{13}\text{N}\) in n-butyl nitrite.

3. Nuclear Quadrupole Relaxation Mechanism. An efficient mechanism for nuclear spin relaxation for nuclei with spin quantum number \(\geq 1\) is the interaction of the nuclear quadrupole moment with the electric field gradient at the nucleus. Nuclei with spin \(\geq 1\) have an asymmetrical distribution of electric charge. This nonspherical charge symmetry gives rise to an electric quadrupole moment, which couples with the time-dependent electric field gradient (due to molecular motion) of the asymmetric distribution of electronic charge about the nucleus) resulting in a relaxation pathway.

Within the limit of motional narrowing the spin-lattice relaxation time as a result of the quadrupolar interaction can be calculated from the following equation:

\[
1/T_{1Q} = \frac{3}{40r^2 (2I - 1)} \left[ \left( \frac{1 + \epsilon^2}{3} \right) \left( \frac{e^2qQ}{\hbar} \right) \right]^2 \tau_c
\]

where \(I\) is the nuclear spin quantum number, \(\epsilon\) is the asymmetry parameter, \(e^2qQ/\hbar\) is the effective quadrupole coupling constant, and \(\tau_c\) is the same molecular correlation time used in calculating the dipolar spin-lattice relaxation time (\(10^{-11}\) to \(10^{-12}\) s for liquids).

In general, for a molecular system containing a quadrupolar nucleus, the measured spin-lattice relaxation time can be used to calculate the molecular correlation time if the effective quadrupole coupling constant is known or has been determined independently. The effective quadrupole coupling constant can be determined by nuclear quadrupole resonance and microwave spectroscopy for solid and gaseous samples, respectively.

The nuclear quadrupole spin-lattice relaxation time depends on the charge symmetry about the quadrupolar nucleus and on the covalence of the chemical bond. For small free ions the electric field gradient (eq) is small, and thus the quadrupolar coupling constant is also small in magnitude. The electric field gradient increases with the increase in the covalent nature of the chemical bond, and thus the quadrupolar coupling constant also increases. For a highly symmetrical molecule or ion (\(\text{NH}_4^+, \text{OH}_2^-, \text{I}^-\)) the quadrupole coupling constant (\(e^2qQ/\hbar\)) is zero and independent of the covalent nature of the bond. A zero quadrupole coupling constant results in long relaxation times (\(\text{NH}_4^+, T_1 = 50\) s; \(\text{BH}_4^-, T_1 = 10\) s)\(^{21, 32}\) \(^{14}\text{N}\) and halogens such as \(^{35}\text{Cl}\), \(^{79}\text{Br}\), and \(^{81}\text{Br}\) in a highly unsymmetrical environment have very short

![FIG. 5. Temperature dependence of the \(^{13}\text{N}\) spin-lattice relaxation time for n-butyl nitrite. From Lambert and Netzel.]

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relaxation times (e.g., CH$_3$C$^{14}$N, $T_1^0 = 22$ ms$^{38}$ and $^{35}$ClO$_4$, $T_1^0 = 1.43$ ms$^{34}$).

4. Scalar Coupling Relaxation Mechanism. The scalar coupling or spin-spin splitting between nuclei with spins $I$ and $S$ observed in high resolution NMR can provide a direct pathway for spin-lattice relaxation. This mechanism differs from the nuclear dipolar coupling interaction in that the relaxation mechanism for a nucleus with spin $S$ depends on the coupling interaction through the bonding electrons with a nucleus with spin $I$ (Fermi hyperfine coupling). The relaxation of a nucleus with spin $S$ can depend on either the time dependence of the coupling constant, $J$, or the relaxation time of a nucleus $I$. In the first case, the time dependence of the coupling constant which gives rise to fluctuating magnetic fields at nucleus $S$ can be the result of chemical exchange or internal rotation of nucleus $I$. This process is referred to as scalar-relaxation of the first kind.

If nucleus $I$ has a spin $> 1/2$, the relaxation time is primarily due to the quadrupole interaction (see Section I B 3). This interaction is an extremely efficient relaxation mechanism resulting in very short relaxation times for nucleus $I$. Rapid relaxation of nucleus $I$ results in fluctuating local magnetic fields at nucleus $S$, thus providing a relaxation mechanism that is referred to as scalar relaxation of the second kind.

The equations for scalar coupling of the first and second kind are identical even though the source of the time dependence of the local magnetic field differs. The equation is as follows:

$$1/T_1^{SC} = \frac{8\pi^2J^2H_0^2I(I+1)}{3(1+(\omega_S - \omega_I)^2\tau_{SC}^2)}$$

where $J$ is the coupling constant, $\omega_I$ and $\omega_S$ are the resonance frequencies for nuclei $I$ and $S$, respectively, $I$ is the nuclear spin quantum number for nucleus $I$, and $\tau_{SC}$ is the correlation time for scalar coupling. If the scalar relaxation is due to chemical exchange or internal motion of nucleus $I$, $\tau_{SC}$ is the chemical exchange time $\tau_e$ which is related to the rate constant for a first-order or pseudo-first-order exchange process ($1/k = \tau_e$). As indicated by Eq. (13), the scalar coupling relaxation mechanism will be inefficient for very fast or very slow exchange processes and will be most efficient when $(\omega_S - \omega_I)^2\tau_e^2 = 1$. Under this condition the scalar coupling relaxation time will be dependent on the magnitude of the external magnetic field through the $(\omega_S - \omega_I)^2$ term. Scalar coupling relaxation can be an efficient mechanism independent of the external magnetic field if the limit of motional narrowing applies (e.g., $\Delta \omega^2\tau_{SC}^2 \ll 1$) and if the coupling constant $J$ is large.

If nucleus $I$ is quadrupolar (e.g., $I > 1/2$) the scalar coupling correlation time $\tau_{SC}$ is equal to the spin-spin quadrupolar relaxation time $T_2^Q$. Analogous to the chemical exchange process, the mechanism for scalar coupling of the second kind will be most efficient and field dependent when $(\omega_S - \omega_I)^2T_2^Q = 1$.

The scalar coupling relaxation mechanism has been found to be significant for the relaxation of $^{31}$P in PBr$_4$ by the quadrupolar nuclei $^{79, 81}$Br and for the relaxation of $^1$H covalently attached to $^{14}$N and $^{11}$B nuclei. However, because of their short relaxation times chlorine and bromine nuclei attached to $^1$H contribute little to the over-all relaxation of the $^1$H nuclei. On the other hand, scalar relaxation of $^{13}$C by $^{35}$Cl, $^{79}$Br, $^{81}$Br, $^{127}$I, and $^{14}$N has been found to be important.

Levy et al.$^{36}$ investigated the relaxation mechanisms for 1-bromocyclohexane and found that the predominant mode was dipolar for all carbon atoms, but that the scalar coupling interaction accounted for 35 to 50% of the relaxation mechanisms for the carbon atom with the bromine substituent ($T_1 = 5$ s). Other ring carbons had relaxation times ($T_1 = 6$ to 8 s), about one-third the value of cyclohexane. In general, if the scalar coupling correlation time resulting from chemical exchange or quadrupolar nuclei is less than $10^{-3}$ s the scalar relaxation mechanism is negligible.

5. Chemical Shift Anisotropy Relaxation Mechanism. An anisotropic distribution of electrons about a nucleus gives rise to chemical shift anisotropy. That is, the chemical shift of a nucleus depends upon the molecular orientation in an external magnetic field. In liquids, because of rapid molecular tumbling the directional components of the shielding tensor are averaged. Thus, only the isotropic chemical shift is observed. The chemical shifts due to anisotropic distribution of electrons about a nucleus can be seen readily in a spectrum of solid compounds. Fig. 6 shows the $^{15}$N chemical shift anisotropy effect for solid nitrobenzene.$^{21}$

Even though the chemical shift anisotropy is averaged for compounds in the liquid state, the rotation of the molecule modulates the local magnetic field due to the anisotropic distribution of electrons about the nucleus and thus provides a mechanism for spin-lattice relaxation.

The theoretically derived equation for the relaxation time due to chemical shift anisotropy is as follows:

$$1/T_1^{CSA} = \frac{\gamma^2H_0^2(\sigma_{12}^2 + \sigma_{13}^2 + \sigma_{23}^2)\tau_e}{5(1 + \omega^2\tau_e^2)}$$

where $\sigma_{ij}$ is the principal value of the anisotropic chemical shielding tensor and the other terms have their usual meaning.

In the case where a molecule has axial symmetry and its molecular motion is in the limit of extreme narrowing, Eq. (14) reduces to

$$1/T_1^{CSA} = \frac{(2/15)\gamma^2H_0^2(\sigma_{11} - \sigma_{12})^2\tau_e}{(1 + \omega^2\tau_e^2)}$$

where $\sigma_{11}$ and $\sigma_{12}$ are the parallel and perpendicular components of the chemical shielding tensors, respect-

![Fig. 6. The $^{15}$N chemical shift anisotropy effect for solid nitrobenzene. (From Schweitzer and Spiess.$^{21}$)](image-url)
tively. Experimentally the term \((\sigma_1 - \sigma_\perp)\) can be obtained from the difference in the parallel and perpendicular chemical shift parameters of the material in the solid state.

The chemical shift anisotropy relaxation mechanism is field dependent and is seldom found for protons because of the small chemical shift range and the low magnetic field strengths of most spectrometers (14 to 23 kG). For nuclei such as \(^{13}\)C, \(^{15}\)N, \(^{19}\)F, and \(^{31}\)P, which have large chemical shift ranges and with newer superconducting magnet spectrometers, relaxation by chemical shift anisotropy can be significant. Since this relaxation time depends on the same molecular correlation time as the dipolar relaxation, lowering the temperature of the sample will also increase the efficiency of the chemical shift anisotropy relaxation mechanism.

\(^{19}\)F in CHFCl\(_2\) is one of the best unambiguous examples of relaxation due to chemical shift anisotropy.\(^{97}\) Chemical shift anisotropy was also found to be an important mechanism for the relaxation of \(^{15}\)N in pyridine at low temperatures and high magnetic fields.\(^{29}\)

6. Separation of the Relaxation Mechanisms. In extracting information about molecular interactions and dynamics via relaxation studies, it is necessary to know the various mechanistic pathways available for a particular molecular system. The observed spin-lattice relaxation rate is the sum of the rates of the individual relaxation mechanisms as shown in Eq. (16):

\[
R_{1 \text{obs}} = R_{1 \text{DD (intra)}} + R_{1 \text{DD (inter)}} + R_{1 \text{SA}} + R_{1 \text{SC}} + R_{1 \text{Q}}
\]

where \(R_{1 \alpha} = 1/T_{1 \alpha}\). Cross correlation between relaxation processes can usually be ignored. If each of the mechanisms described contributes to the observed relaxation time, the task of differentiating and determining each contribution is exceedingly difficult. Fortunately in most cases several of the relaxation pathways may be insignificant or completely absent. Numerous investigations\(^{31, 34, 36-47}\) have been reported in which various combinations of mechanisms have been separated and the contribution determined using variable temperature, variable frequency, and the nuclear Overhauser effect (NOE) measurements.

For \(^{13}\)C and other nuclei that have a positive gyromagnetic ratio, the intramolecular dipolar relaxation contribution to the over-all observed relaxation rate can easily be determined from measurements of the NOE\(^{3}\) resulting from decoupling experiments. Intense decoupling irradiation of nuclei attached to the nuclei under observation results in an excess spin population of the observed nuclei in the lower energy level, and thus a corresponding enhancement in the resonance signal. Maximum NOE enhancement \((1 + \eta)\) will occur only if intramolecular dipolar relaxation is the sole mechanism. NOE enhancements less than the theoretical maximum indicate that other relaxation mechanisms are present. If the experimental NOE \((1 + \eta_{\text{obs}})\) is determined from the ratio of the intensity of the decoupled and undecoupled resonances, \(A_d/A_u\), the contribution of the dipolar mechanism to the total relaxation time can be calculated (see Eqs. (17) to (20)):

\[
A_d/A_u = 1 + \eta_{\text{obs}}
\]

\[
\eta_{\text{obs}} = A_d/A_u - 1
\]

\[
\text{fraction of dipolar relaxation} = \frac{\eta_{\text{obs}}}{\eta_{\text{max}}}
\]

\[
T_{1 \text{DD}} = T_{1 \text{obs}} \left(\frac{\eta_{\text{max}}}{\eta_{\text{obs}}}\right)
\]

For proton decoupled \(^{13}\)C, the theoretical NOE \((\eta_{\text{max}})\) is 1.988. Nuclei such as \(^{13}\)N and \(^{29}\)Si have negative gyromagnetic ratios and thus, proton decoupling experiments for these nuclei lead to NOE enhancements that may result in a fully inverted enhanced resonance signal if only the dipolar mechanism is operating. Partially inverted, zero, or positive resonance signals may result if other mechanisms are significant to the relaxation process.\(^{46, 49}\)

The temperature and viscosity dependence of the spin-rotation interaction is opposite to that of the dipolar interaction and thus provides a means by which the contribution of each of these mechanisms to the overall relaxation time can be determined. If both mechanisms operate in a molecular system, the dipolar mechanism will dominate at low temperatures and the spin-rotation at high temperatures. When both mechanisms are contributing equally to the relaxation rate a maximum will be observed in a plot of the observed relaxation time vs the reciprocal of the absolute temperature, as shown in Fig. 7.

The chemical shift anisotropy relaxation time is field (frequency) dependent and thus can be separated readily from other relaxation mechanisms by determining the relaxation time as a function of the magnetic field strength at constant temperature. However, as was pointed out in Section I B 4, the scalar coupling relaxation mechanism in certain situations can depend on the strength of the magnetic field, and if this mechanism contributes significantly to the total relaxation rate, separating the scalar coupling from the chemical shift anisotropy mechanism can be extremely difficult.

Evidence for or against quadrupole relaxation can usually be obtained from inspection of the resonance spectra. If quadrupole relaxation dominates, the mechanism will be very efficient and scalar coupling or spin-spin coupling between the nuclei will not be observed and a single resonance line will result. The proton spectrum of \(^{15}\)NH\(_3\)\(^+\), which has tetrahedral symmetry and a zero quadrupole coupling constant, shows a sharp quintet of lines whereas the proton spectrum of \(^{14}\)NH\(_3\) shows...
a single broad resonance line indicating that the relaxation of the $^{14}$N nucleus due to the quadrupole interaction is far too rapid for scalar coupling to occur.

If care is taken to prepare a sample so that paramagnetic impurities are reduced to negligible amounts (e.g., degassing the sample to remove oxygen, ion exchange or EDTA treatment to remove metallic ions), the intermolecular dipolar interaction can be significantly reduced as a possible relaxation pathway.

II. RELAXATION TIME MEASUREMENTS

A. Instrumentation. Relaxation data can be obtained on both high resolution and wideline spectrometers operating in either the continuous wave (CW) or the pulse mode. Because of the convenience and availability of pulse Fourier transform NMR spectrometers, almost all relaxation studies are now conducted on computerized pulse spectrometers. Pulse spectrometers require a relatively powerful rf transmitter, a pulse programmer to gate the transmitted frequency to produce a pulse, a single-coil sample probe, a receiver that has a very short recovery time after being saturated by the rf pulse, a disc-based data acquisition system, and a computer for calculating the Fourier transforms, for controlling the instrumental parameters after the initial setup, for calculating relaxation times, and for plotting and/or printing the results.

The major advantages of the pulse technique over the CW mode of operation are (1) rapid relaxation data acquisition for all like nuclei within a molecule, and (2) versatility in experimental technique.

Discussion of the instrumental and computing requirements for pulse Fourier NMR spectrometers can be found in several of the reviews that have been written on Fourier transform spectroscopy.8-50-63

B. Free Induction Decay. The receiver coil of a pulse spectrometer lies on one of the axes in the $x'y'$ plane perpendicular to the external magnetic field. Thus any magnetization component of the nuclear spins in the $x'y'$ plane results in an observed signal. Because of spin-spin relaxation and magnetic field inhomogeneity, the signal decays at a rate $1/T_2^*$ (see Section I A). The decay of the signal (illustrated in Fig. 8) is referred to as the free induction decay (FID) and is the time domain spectrum of the sample. The initial amplitude of the signal is directly related to the magnitude of the magnetization vector, $M_0$. The familiar NMR absorption spectrum or frequency domain spectrum may be obtained through the use of the mathematical Fourier transformation operation (see Section III B 1).

C. Spin Lattice Relaxation Times. A number of techniques are available to measure the spin-lattice relaxation times. Older literature describes the use of the rapid passage adiabatic process.4 However, with the advent of pulse Fourier transform spectroscopy, inversion recovery,54 progressive saturation,55,56 saturation recovery,57 intensity ratios,58 and null59 methods have been used to determine spin-lattice relaxation times experimentally. A number of reviews on the subject can be found in the literature.8-9,60,61

For completeness a brief description of two methods and of the factors affecting the relaxation experiment will be discussed.

1. Inversion Recovery. This technique is the most commonly applied pulse sequence method for measuring relaxation times and is represented by the following notation: $(180^{\circ}-t-90^{\circ}-T)$, where $180^{\circ}$ and $90^{\circ}$ are the angles the magnetization vector is rotated after an intense rf pulse, $t$ is the time between pulses, and $T$ is the delay time before repeating the sequence of pulses. It is necessary for the reestablishment of the Boltzmann distribution of spins that the delay time be 4 to 5 times the longest relaxation time measured in a molecular system. Fig. 9 shows diagrammatically the effects of the noneselective $180^{\circ}$ and $90^{\circ}$ pulses on the nuclear spin magnetization vector, $M_0$.

Initially the net magnetization vector is aligned parallel to the direction of the magnetic field as shown in Fig. 9A. After an intense $180^{\circ}$ rf pulse (Fig. 9B), the magnetization vector lies in the $-z'$ direction (inversion of the spin populations).

Immediately after the $180^{\circ}$ pulse the $z'$ component of the magnetization vector begins to decrease in magnitude (Fig. 9C), becomes zero and then increases to the equilibrium value of $M_0$ along the $+z'$ axis. The rate of change in the magnitude of the $z'$ component of the magnetization vector is dictated by the spin-lattice relaxation time of the nuclear spin. If after a certain amount of time, $t$, a $90^{\circ}$ pulse is introduced, the magnetization vector, $M_{z'}(t)$, will be rotated into the $x'y'$ plane.
The magnitude of the nuclear spin magnetization is recorded as the initial height of the observed FID. The Fourier transform of this time domain spectrum produces the frequency domain spectrum, in which the amplitude of the resonance signals represents the number of spins that have not yet fully relaxed after a time, t. Fig. 10 shows a stack plot of the $^{13}$C NMR spectra of 1-methylpiperidine recorded at various $t$ values. One second after the 180° pulse all resonances are negative ($t < T_1$). Between 10 and 15 s the signals are nulled ($t = T_1$) and after 100 s ($t > T_1$) complete establishment of the Boltzmann distribution has occurred and the signals are positive with full intensity.

The amplitude, $M_t$, for each individual resonance line after a time interval, $t$, is given by the following equation:

$$M_t = M_0 (1 - 2e^{-t/T_1})$$

(21)

where $M_0$ is the amplitude of the resonance signal after a single 90° pulse. To calculate $T_1$ from the amplitude data, Eq. (21) is rearranged as follows:

$$\ln (M_0 - M_t) = \ln 2M_0 - t/T_1$$

(22)

Thus, a semilog plot of the differences in amplitudes vs pulse interval time results in a straight line with a slope equal to $-1/T_1$. Fig. 11 shows the application of Eq. (22) for determining the relaxation time for benzene. Computation of the spin-lattice relaxation time using Eq. (22) is very dependent upon the intensity of the signal after the 90° pulse ($M_0$) and weighting errors inherent in semilog plots when $t$ values greater than $1.5T_1$ are used. A listing of a computer program for calculating $T_1$ and plotting the data as shown in Fig. 11 can be found in the thesis by Netzel. 62

A better method for calculating $T_1$ values uses an exponential least-squares regression program in treating the data. Fig. 12 illustrates the results obtained using such a program for computing $T_1$ for the $\beta$-carbon of 1-methylpiperidine. The intensity $M_t$ is plotted against the pulse interval time, $t$, and the best exponential fit of the data is determined. Unlike the semilog plot method, this computation of $T_1$ is independent of $M_0$. Also experimental time is shortened since $M_0$ need not be determined. A computer program for calculating $T_1$ by this method can be found in the thesis by Netzel. 62

The program is written in BASIC and computes the best exponential curve to the data points according to the least-squares criterion by adjusting $M_t$, the intensity of signal after a 180° pulse; $M_0$ the intensity of the signal after an infinite time (a 90° pulse), and $T_1$, the spin-lattice relaxation time. The only input data that are required are the intensities of the signals, $M_t$, and the pulse interval time, $t$. The program lists the spin-lattice relaxation time, the number of iterations, the theoretical intensity at a given $t$, the difference between the computed intensity and the observed intensity at a given $t$, the standard deviation for the best fit, the 90° error estimate of $T_1$ in seconds and percent, and the computed intensity at infinite time, $M_0$.

If two or more resonance signals have the same chemical shift or if the resonance signals cannot be resolved, a semilog plot of the amplitude data vs pulse interval time will show a nonlinear relationship. This is often the case when industrial products are investigated. If only two resonance signals overlap and their relaxation times are sufficiently different, the semilog plot will show two distinct regions from which the individual relaxation times can be determined. Systems in which the relaxation times are not sufficiently different and/or the chemical shifts are not resolvable for a multi-component mixture, extraction of individual relaxation times is not possible. The interpretation of the relaxation data in terms of molecular dynamics will result in only a molecular average for the system.

The greatest single disadvantage of the inversion-recovery technique is the long delay time necessary to repeat the pulse sequence. This is especially true for those nuclei that have relaxation times in excess of 30 s. The time problem is compounded if the amount of material dictates the use of extensive time averaging of the data to achieve sufficient signal/noise ratio. Fortunately, after the initial setup, relaxation investigations are computer controlled and thus, the data can be obtained in the late hours of the evening or over weekends.
without the presence of the operator. Because of the long times that may be necessary to obtain reliable relaxation time data, instrumental reliability is also a problem.

Freeman and Hill\(^6^3\) have developed the pulse sequence \((T-90^\circ-T-180^\circ-T-180^\circ-T)^*\), in an effort to overcome instrument drift in resolution and/or gain. In this sequence the normal inversion-recovery pulse sequence is preceded by a single isolated 90° pulse. In the computation of the relaxation time, the computer records the FID for the 90° pulse and subtracts the FID of the 90° monitoring pulse. The resulting FID is Fourier transformed and the amplitude of the resonance signals in the frequency domain spectra represents the function \(M_0 - M_t\) directly. Measuring the amplitudes of the signals for the 90° pulse and subtracting from it the amplitude of the relaxed signals minimizes the errors due to long-term drift in the spectrometer operation.

2. Progressive Saturation. To circumvent the long delay times necessary to obtain \(T_1\) data using the inversion-recovery technique, Freeman and Hill\(^6^3\) proposed a sequence of equally spaced 90° pulses to achieve a steady-state condition for the population of the nuclear spins in lower and higher energy states. If the spacing between pulses is very short compared to \(T_1\) \((t < T_1)\), near equalization of the spin populations in the energy states will occur; that is, the system will be saturated and thus the amplitude of the resonance signal will be near zero. Increasing the pulse interval time will increase the steady-state amplitude of the resonance signal. Starting with very short \(t\) values and observing the amplitude of the resonance signal as \(t\) is increased eliminates long delay times. The amplitude of the signal is given by the following expression:

\[
M_t = M_0(1 - e^{-t/T_1})
\]

The spin lattice relaxation time can be calculated from either the semilog plot of \(M_0 - M_t\) vs \(t\) or the exponential plot.

Operationally the first several FID values are not collected by the computer. Only those pulses corresponding to a steady-state condition are time averaged until a suitable signal/noise ratio has been attained. This technique, however, has disadvantages: (1) immediately after a 90° pulse the nuclear spin magnetization vector must be in the \(x'y'\) plane; that is, the 90° pulse must be accurately set; and (2) before the next 90° pulse residual magnetization due to slow spin-spin relaxation must be absent. This last condition can be realized if a "homospoil" pulse is applied to a sample to cancel residual \(x'y'\) magnetization before the next 90° pulse.\(^5^7\) However, use of a homospoil pulse places a lower limit on the relaxation times that can be measured.

3. Factors Influencing Relaxation Measurements. Factors that affect the relaxation experiment can be divided into two categories—instrumental and sample preparation. Without careful attention to the various factors, erroneous relaxation times and/or nonexponential relaxation rates that are not characteristic of the sample may be observed. Proper choice of a pulse sequence will also allow optimization of experiment time for relaxation measurements. An excellent discussion on the experimental approach to accurate spin-lattice relaxation measurements for the various pulse techniques has recently been published by Levy and Peat.\(^6^1\)

Instrumentally, relaxation times are affected by the homogeneity of the external and rf magnetic fields, the strength of the rf pulse to effectively flip the spins, the electronic stability of the pulse system, the effective decoupling power, data processing, and the limitation of the computer.

Relaxation times are strongly influenced by sample preparation. Paramagnetic impurities in the sample are the greatest deterrents to the measurement of true relaxation times. Oxygen must be removed by degassing if relaxation times are greater than 5 to 10 s. Relaxation times of dissolved solids and dilute liquids will depend on the choice of solvent (because of intermolecular interactions, changes in the viscosity of the system, etc.). Consideration must also be given to a loss of spins from

Fig. 12. A plot of the intensity \(M_t\) vs \(t\) for the determination of \(T_1\) for the \(\beta\)-carbon of 1-methylpiperidine at 303°K. (From Netzel.\(^4^2\))

\[
\text{Intensity (Digital Readout \times 10^{-3})}
\]

\[
\text{Pulse Interval (sec)}
\]

\[
\text{Experimental Data}
\]

\[
\text{Exponential Least Squares Fit}
\]
the receiver coils through diffusion effects or volatility of the samples. These effects can be minimized easily by proper design of the NMR tube. Diffusion is not a serious factor for relaxation times less than 50 s.

Of considerable importance is the temperature control when relaxation times are measured. Variations of 3 to 5°C can lead to changes up to 16% for $T_1$. Diffusion is not a serious factor for relaxation times less than 50 s. Of considerable importance is the temperature control when relaxation times are measured. Variations of 3 to 5°C can lead to changes up to 16% for $T_1$.

D. Spin-Spin Relaxation Time. The spin-spin relaxation time cannot be measured as simply as the spin-lattice relaxation time because of inhomogeneity effects of the magnetic field and molecular diffusion within the sample. The magnetic inhomogeneity effect on $T_2$ can be overcome by using the spin echo technique. This technique consists of a pulse sequence of 90°-t-180°, which produces an echo signal at a time $2t$. An echo appears as a consequence of the constructive interference of the nuclear spin moments under the influence of the second pulse. Fig. 13 gives an illustration of a spin-echo FID after several consecutive 180° pulses.

How a nuclear spin system responds to a 90° pulse followed by a 180° pulse and the formation of an echo is illustrated in Fig. 14. The illustrations are based upon the rotating frame of reference coordinate system. The magnetization vector is rotated 90° by the pulse (Fig. 14, A to C). At the end of the pulse, phase coherence is lost due to spin-spin relaxation and field inhomogeneity (Fig. 14D). If after a time $t$ a second pulse is applied with a width of $2\tau_m$ (a 180° pulse), the vectors are rotated through 180° about the $x'$ axis (Fig. 14E). The individual vectors continue to move in the same direction as before the 180° pulse but now instead of "fanning out" they begin to refocus (Fig. 14F). At a time $2t$ the vectors will have completely coalesced, resulting in a strong signal or "echo" in the receiver coil (Fig. 14G). The decay of the echo signal occurs by the same mechanisms as described previously (Fig. 14H).

Effects due to the field inhomogeneity on $T_2^*$ are eliminated because these effects are reversible under the action of the pulses. By varying the spacing between the 90° and 180° pulses, the echo amplitude, $M_e$, will be observed to decay with the form,

$$M_t = M_0 e^{-2\tau T_2}$$

(24)

The computation of $T_2$ is analogous to the procedure described for the $T_1$ inversion-recovery technique (Section II C 1).

A true $T_2$, governed by Eq. (24) still may not be measurable by the 90°-t-180° sequence if molecular diffusion occurs and dominates the $T_2$ relaxation process. For these situations the amplitude of the echo takes the following form:

$$M_t = M_0 e^{-2\tau T_2} e^{-2g\tau T_2 D}$$

(25)

where $g$ and $D$ are the magnitude of the field gradient and the coefficient of self-diffusion, respectively. Here the amplitude of the echo is dominated by a $\epsilon^2$ dependence of the second term and exhibits a cubic rather than a linear dependence when plotted semilogarithmically. Application of pulse sequences drastically reduces diffusional effects and allows $T_2$ to be measured. Examples are the Carr-Purcell and Meiboom-Gill pulse sequences.

The Carr-Purcell pulse sequence is as follows: 90°-t-180°-2t-180°-2t-180°-t. A disadvantage of this technique is that for long $T_2$ many 180° pulses are necessary and any error in the length of the pulses results in incomplete rephasing of the nuclear moments. Meiboom and Gill modified the Carr and Purcell spin-echo technique by using successive coherent pulses and shifting the phase of the 90° pulse by 90° relative to the phase of the 180° pulse. These modifications eliminated the necessity for very accurate adjustment of the 180° pulses and thus improved the reproducibility of $T_2$ measurements.

III. APPLICATIONS

Relaxation time measurements have been used extensively in probing the structure and behavior of matter. It is not possible in this article to review all of the applications for which relaxation time measurements have been used. Several good reviews have appeared in the literature which discuss the applications of $^{13}$C spin-lattice relaxation times to investigations of molecular structure, dynamics, and interactions.4-6, 67-70
A. Physicochemical Properties of Molecules.

1. Molecular Structure, Conformation, and Intramolecular Steric Hindrance. The rate of relaxation for dipolar interaction depends on the inverse sixth power of the internuclear bond length and on the number of nuclei directly or indirectly attached to the nucleus of interest. By noting the differences in the magnitude of the dipolar relaxation times for the various nuclei within a molecule, spectral assignment of the resonances can be made that generally will confirm the structure. 

$^{13}$C spin-lattice relaxation studies have been used to distinguish between methine, methylene, and nonprotonated $^{13}$C atoms in spectra of complex molecules. If the dipolar relaxation mechanism is the predominant mode and the molecule is rotating isotropically, the relaxation times for methine and methylene carbons will be inversely related to the number of attached protons (see Eq. (8)). Thus the ratios $T_1^{\text{CH}}/T_1^{\text{CH}_2}$ will be about 2:1. Methyl groups cannot be determined by a simple ratio based on the number of protons since in general, the group is free to rotate. The internal rotation of the methyl group increases the $^{13}$C dipolar relaxation time relative to the methine and methylene carbons. Nonprotonated $^{13}$C nuclei are readily assigned because of their long relaxation times relative to carbon atoms having attached hydrogens. 1,1-Dimethylcyclohexane serves to illustrate the point. The methyl and the C-1 carbon atoms have similar chemical shifts (29.4 and 30.6 ppm, respectively). However, the $^{13}$C relaxation times have been found to be 8.4 and 70.0 s for the methyl and C-1 atoms, respectively, and thus provides an unambiguous assignment to be made.

The assignment of several nonprotonated carbon atoms within a molecule can be made by comparing the measured relaxation times and noting the effects of long range intramolecular dipolar interactions. Levy et al. measured the $^{13}$C relaxation times for mescaline (Fig. 15), which has three types of nonprotonated carbons. The quaternary carbon with a relaxation time of 14.2 s was assigned to the aromatic C-4 position since long range intramolecular dipolar interactions are insignificant. Both C-3 and C-5 have one adjacent ortho proton and thus have shorter relaxation times (11.1 s). The shortest relaxation time (4.2 s) can be assigned to the quaternary carbon C-1, since it has two adjacent ortho protons as well as long range intramolecular dipolar contribution from the protons of the attached methylene group.

Selective deuteriation in conjunction with $^{13}$C $T_1$ measurements have also been useful in spectral assignment. $^{13}$C relaxation times are significantly increased when deuterium nuclei replace directly bonded protons. Relaxation times for completely deuterated carbons are comparable to nonprotonated carbons. Nonprotonated carbon relaxation times are also affected by deuterium substitution on adjacent carbons. The relaxation times of the olefinic carbons C-7a and C-12a in the alkaloid (Fig. 16) were increased when deuterium was substituted for hydrogen at C-7 and C-12b.

Allerhand et al. used the inversion-recovery technique as an aid in assigning the $^{11}$B resonances in the spectra of decaborane(14) and a nonaborane(15). The normal NMR spectrum of decaborane(14) is shown in Fig. 17A. The downfield triplet could be the result of one BH$_2$ group or an overlap of two BH doublets. Readily apparent from a stack plot of the spectra A to G, the downfield triplet of decaborane(14) is shown to be resolved into two overlapping doublets as a result of different relaxation times for each $^{11}$B moiety. Allerhand et al. have also shown by $^{11}$B $T_1$ measurements that the previously hidden B(3)H$_2$ triplet in n-nonaborane(15) is hidden under the main body of the $^{11}$B spectrum through accidental overlap of all three peaks with other resonances (Fig. 18, A to F). It is because of the shorter relaxation time for the B(3)H$_2$ moiety relative to the other $^{11}$B nuclei in the same chemical shift region that an unambiguous assignment can be made.

Conformational information on a molecular system can be obtained from relaxation studies by (1) comparing the theoretically calculated relaxation times for a given molecular conformation with the observed $T_1$.

FIG. 15. Mescaline structure and relaxation times.

FIG. 16. 1,2,3,4,6,7,12a,12b-Octahydroindolo[2,3-a]quinolizine.

FIG. 17. Stack plot of the $^{11}$B NMR spectra of decaborane(14). (From Allerhand et al.)
values, and (2) determining the change in relaxation time upon deuterium substitution.

The conformation of the unsymmetrical molecule all-trans retinal (Fig. 19) was studied by Becker et al., using $^{13}$C $T_1$ data. From the observed relaxation times and the assumption of various conformations of the molecule, they were able to calculate (using Woesner's equations) the effect of anisotropic diffusion on $T_1$ in terms of rotational diffusion constants. With the use of these constants and the various values for the dihedral angle between the rigid olefinic chain (C-7, C-8) and cyclohexane ring (C-5, C-6), the relaxation times for each of the carbon atoms in the molecule were calculated. The best comparison of the experimental and calculated $T_1$ data was obtained when a dihedral angle of 60° was assumed.

Specific deuterium substitution of protons within a molecule has also been used to determine the conformation of molecules in solution. The technique is based upon the fact that substitution by deuterium decreases the relaxation rate of the conformationally adjacent proton within the molecule. From the dipolar proton differential relaxation rate $1/T_1({}^1H, {}^2H) - 1/T_1({}^1H, {}^1H)$ and the molecular rotational correlation time, $\tau_c$, obtained from $^{13}$C spin-lattice relaxation measurements; the inverse sixth power-averaged interproton distances were calculated and the conformation was postulated. The relationship between the average interproton distance and the differential relaxation rate is given in Eq. (26):

$$1/T_1({}^1H, {}^1H) - 1/T_1({}^1H, {}^2H) = \frac{3}{2} \gamma_1 h^2 \tau_c r^6 + \frac{1}{2} \gamma_1^2 h^2 \tau_c r^{-6}$$

where $1/T_1({}^1H, {}^1H)$ is the proton relaxation rate before selective deuteration and $1/T_1({}^1H, {}^2H)$ is the proton relaxation rate after deuteration of one of the pair of protons. The other terms have their usual meanings. The second term in Eq. (26) arises because $^2H$ can reduce significantly the dipolar contribution when the interproton distance is at a minimum.

This technique has been applied to some purine nucleoside derivatives by Akasaka et al., and to nicotinamide mononucleotide by Zens et al. In the paper by Zens et al., the differential relaxation rates and spin-lattice relaxation times were calculated from a rotational correlation time and the interproton distances were estimated from x-ray data for various conformations of the molecule and compared to the experimentally determined relaxation times.

Aside from the examples cited above, spin-lattice relaxation times do not, in general, directly define the preferred conformation of a molecule. However, if a functional group is sterically hindered, the energetics of the preferred conformer can be discussed qualitatively. A series of methyl-substituted aromatic compounds shown in Fig. 20 is used to illustrate the point.

In toluene (Fig. 20A) the methyl group is free to rotate about the carbon-carbon bond and has a $^{13}$C $T_1$ value of 16.3 s. On the other hand the peri-hydrogen in 1-methylnaphthalene (Fig. 20B) sterically hinders the methyl rotation forcing the methyl group to assume a preferred conformation and resulting in a faster relaxation time of 5.8 s. In the sterically unfavorable case of 9-methylanthracene (Fig. 20C) the two peri-hydrogens interact equally with the methyl group so that no preferred conformation occurs, as is evident by the longer relaxation time (14.0 s).

The effects of nearly equal van der Waals interactions on the rotation of the methyl group are also noted in the two isomers of 2-butanone oxime (Fig. 21). In isomer A, the methyl group is forced into a preferred conformation resulting in a short $^{13}$C relaxation time of 2.8 s. The longer relaxation time of 6.1 s for the methyl group in isomer B suggests that (1) the methylene and hydroxy-
imino groups interact with the methyl group to about the same extent, and (2) no preferred conformation exists for the methyl group even though the methyl group appears to be more sterically hindered than in isomer A.

The barrier to rotation for intramolecular sterically hindered methyl groups can be determined from variable temperature and NOE studies of $^{13}$C relaxation times.78.79

2. Molecular Association. Intermolecular association of molecules in solution such as hydrogen bonding, solvation, and complex formation can be investigated by noting the changes in the molecular rotational correlation time $\tau_r$ as a function of concentration and temperature. The correlation time is directly related to the size of the molecule and, thus, if association occurs, $\tau_r$ will increase resulting in a shorter $T_1$ value. The observed relaxation time may be the sum of several mechanisms if the solution contains small molecules. Therefore, before one can attempt to correlate the measured relaxation times to intermolecular association, the extent of each type of mechanism present must be assessed. The important mechanisms are dipolar, spin rotation, and scalar relaxation of the first kind. If nuclei with a quadrupole moment are investigated, the $T_1$ can be used directly to determine the extent of association since the correlation time for this mechanism is the molecular reorientation time $\tau_r$.

Inlow et al.80 used $T_1$ measurements to study the hydrogen bonding properties of CD$_3$OH and CH$_3$OH in solvents of varying hydrogen bonding abilities. They found that extrapolation of the spin-lattice relaxation time to infinite dilution gives an indication of the strength of the alcohol-solvent hydrogen bond. Tucker et al.81 investigated the hydrogen bonding properties of t-butyl alcohol in $n$-hexadecane-d$_{82}$ and CCl$_4$ using $^{13}$C spin-lattice relaxation data of the carbinox carbon. The relaxation time was found to increase substantially as the alcohol was diluted with either solvent indicating a decrease in hydrogen bonding. With the 1-3-6 association model, the percentages of t-butyl monomer, trimer, and hexamer were calculated from the relaxation data.

Morgan and Van Wazer82 using $^{31}$P spin-lattice relaxation data studied the molecular species obtained when titrating a dilute solution of aqueous orthophosphoric acid with tetramethylammonium hydroxide. The predominant relaxation mechanisms for phosphorus were considered to be (1) the interaction of $^{31}$P nuclear spins with the molecular rotation, and (2) dipolar interaction between pairs of $^{31}$P nuclei or between $^{31}$P and $^1$H nuclei. Scalar relaxation of the first kind due to exchange of protons between the oxyacid and the solvent water was also considered in their investigation. Relaxation due to chemical shift anisotropy was shown not to be a factor for the compound used in the study.

A pH titration plot (Fig. 22) of the $^{31}$P relaxation time vs the pH of a 0.2 M orthophosphoric acid solution shows an oscillatory variation of the $T_1$. The maxima in the oscillatory curve appeared at the pH corresponding to the individual species PO$_4^{3-}$, HPO$_4^{2-}$, H$_2$PO$_4^-$, H$_3$PO$_4$, and, in the presence of concentrated perchloric acid, the PO$_4^{3-}$ species. From a quantitative treatment of the intra- and intermolecular dipolar interactions and with appropriate attention paid to the degree of ionization, the oscillatory behavior of the $T_1$ measurements could be explained adequately. Thus, at a pH value intermediate between two maxima, the observed relaxation rate is the sum of the relaxation rates of the contributing ions.

In systems involving interactions between organic ions, the spin-lattice relaxation times will increase as the dielectric constant of the solvent increases. In solvents of low dielectric constant, ions are weakly solvated and relatively strong interionic association between organic ions increases the molecular size of the species with a corresponding increase in the molecular rotational correlation time. As the dielectric constant of the solvent increases, ionic interactions decrease because of strong ion-dipole solvation of the organic ions. This results in enhanced mobility of the organic molecule and a corresponding decrease in the molecular correlation time.

The influence of solvent polarity on the $^{13}$C relaxation times of n-butylammonium trifluoroacetate is shown in Table I.

The absence of a 1:1 correspondence of $T_1$ to the dielectric constant of the solvent may be due in part to variations in the viscosity of the solution.

The formation of lanthanum complexes in aqueous salt solutions was investigated by Reuben83 using the inversion-recovery technique to measure the quadrupolar spin-lattice relaxation time of the $^{139}$La nucleus. From Eq. (12) and the assumption that the molecular motion of a rigid complex can be described by the diffusion equation of Stokes84 it follows that the relaxation rate should be proportional to the quadrupole coupling constant of $^{139}$La and the viscosity of the solvent. Also, the observed relaxation rate will be the weighted average of the relaxation rate for each complex in solution if rapid exchange occurs between the species present. This situation can be expressed mathematically as

![FIG. 22. $^{31}$P spin-lattice relaxation times as a function of the pH of 0.2 M orthophosphoric acid solution. (From Morgan and Van Wazer.82)](image)

<table>
<thead>
<tr>
<th>Solvent</th>
<th>conc (wt. %)</th>
<th>Spin-lattice relaxation time for carbon atoms (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$\delta$-CH$_3$</td>
</tr>
<tr>
<td>1,4-Dioxane</td>
<td>20</td>
<td>3.35</td>
</tr>
<tr>
<td>CH$_3$Cl/acetone</td>
<td>24</td>
<td>3.90</td>
</tr>
<tr>
<td>CF$_3$COOH</td>
<td>15.4</td>
<td>3.98</td>
</tr>
<tr>
<td>CD$_3$OD</td>
<td>28.4</td>
<td>3.46</td>
</tr>
<tr>
<td>CD$_3$OD</td>
<td>20.0</td>
<td>6.00</td>
</tr>
<tr>
<td>D$_2$O</td>
<td>20.0</td>
<td>5.00</td>
</tr>
</tbody>
</table>

* From Levy.85
\[ 1/T_1^{\text{obs}} = \sum_i X_i / T_1^i \]  

where \( X_i \) is the mole fraction of the \( i \)th complex with a relaxation time of \( T_{1i} \).

A plot of the relaxation rate for \(^{139}\text{La} \) as a function of the concentration of \( \text{LaCl}_3 \) solution shows that the relaxation rate corresponds only to the increase in the viscosity of the solution and not to any molecular association. However, the \(^{139}\text{La} \) relaxation rate for \( \text{La(ClO}_4\text{)}_3 \) solutions was observed to increase faster than that predicted on the basis of viscosity alone. A plot of the \(^{139}\text{La} \) relaxation rates in solutions of \( \text{La(ClO}_4\text{)}_3 \) as a function of various concentrations of \( \text{NaCl} \), \( \text{LiClO}_4 \), and \( \text{LiNO}_3 \) is shown in Fig. 23. The change in the \(^{139}\text{La} \) relaxation rate in \( \text{La(ClO}_4\text{)}_3 \) solution with the addition of \( \text{NaCl} \) corresponds only to a change in the viscosity of the solution. However, the addition of \( \text{LiClO}_4 \) and \( \text{LiNO}_3 \) to a solution of \( \text{La(ClO}_4\text{)}_3 \) increased the \(^{139}\text{La} \) relaxation rate. The large increase in the relaxation rate upon the addition of \( \text{LiNO}_3 \) corresponds to the formation of an inner-sphere nitrate complex. The unexpected relaxation effects arising from the addition of excess perchlorate ion may suggest the formation of an outer-sphere ion pair between the lanthanum aquo-ion and the perchlorate ions. The increase in the relaxation rates observed and thus the increase in \( \tau_r \) due to the increased size of the complexes when the aquo groups are replaced by the large nitrate and perchlorate ions.

Hertz and references cited therein give an excellent discussion of the structure of liquids as studied by nuclear spin relaxation spectroscopy.

3. Molecular Dynamics. In principle, nuclear spin relaxation can be used as a sensitive probe to study the translational and overall rotational motions of a molecule in solution as well as the internal rotation and segmental motions within a molecule. As discussed in Section I the theoretically derived relaxation equations were based upon rigid spherical molecules tumbling isotropically in solution. Anisotropic behavior of molecules in solution has a profound effect on the relaxation rates and the basic equations must be modified to account for the effects. However, relaxation data can be discussed qualitatively and rationalized on the basis of anisotropic and segmental motion.

a. Anisotropic Motion. Anisotropic motion of a molecule can result from inter- and intramolecular interactions; inertial, frictional, and electrostatic effects that depend on the size, polarity, bonding ability, and symmetry of the molecule.

Anisotropic tumbling of a molecule often results in shorter spin-lattice relaxation times for nuclei along the axis of symmetry of the molecule. In monosubstituted benzenes the ortho and meta carbons have \(^{13}C\ T_1\) values that are longer than the spin-lattice relaxation time for the para carbon. This difference occurs because the dipolar interaction of the para carbon with its directly attached proton is not greatly modulated during the rotation around the \( C_3 \) molecular symmetry axis and thus does not shorten the effective correlation time, so that \( T_1 \) is essentially unaffected. Rotation about the \( C_{2v} \) axis, however, does modulate the carbon-hydrogen dipolar interaction of the ortho and meta carbon and bring about longer relaxation times. Large, heavy, or highly polar substituents will cause rotation about the \( C_{2v} \) molecular symmetry axis 5 to 20 times faster than about the perpendicular axes.

Table II lists the spin-lattice relaxation times for the \( \alpha \), \( \beta \), \( \gamma \), and methyl carbons of the pentamethylene heterocycles of groups IV, V, and VI.

A survey of the spin-lattice relaxation times listed in Table II indicates that generally as the size of the heteroatom increases the relaxation times decrease. This trend is quite evident in the saturated group VI heterocycles and was discussed in Section I B 1. Anisotropic tumbling of the molecules in solution as evidenced by the longer spin-lattice relaxation times for the \( \alpha \) and \( \beta \)-carbons compared to the \( \gamma \)-carbon is observed for the heterocycles of groups IV and V. The effect is similar to, but not so large as, that in monosubstituted benzenes.

The preferred axis of molecular rotation therefore is that between the heteroatom and \( C-4 \). For the group VI heterocycles, which have no substituent on \( X \), the relaxation times are almost the same for all the carbons. Tumbling must be essentially isotropic for this entire series.

b. Segmental Motion. The flexibility of long aliphatic molecules results in localized (segmental) motion along the chain that can be observed as variations in the relaxation times. Segmental motion can only be observed, however, if the motion equals or exceeds the magnitude of molecular tumbling.

<table>
<thead>
<tr>
<th>( X )</th>
<th>( \alpha )</th>
<th>( \beta )</th>
<th>( \gamma )</th>
<th>( \text{CH}_3 )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group IV</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( C\text{(CH}_3\text{)}_2 )</td>
<td>11.9 ± 0.6</td>
<td>11.3 ± 0.6</td>
<td>10.4 ± 0.5</td>
<td>8.4 ± 0.9</td>
</tr>
<tr>
<td>( \text{Si(CH}_3\text{)}_2 )</td>
<td>9.6 ± 0.6</td>
<td>9.0 ± 0.5</td>
<td>8.8 ± 0.6</td>
<td>11.6 ± 0.6</td>
</tr>
<tr>
<td><strong>Group V</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \text{NH} )</td>
<td>6.0 ± 1.4</td>
<td>7.6 ± 1.1</td>
<td>6.9 ± 1.1</td>
<td></td>
</tr>
<tr>
<td>( \text{NCH}_3 )</td>
<td>12.8 ± 0.9</td>
<td>12.6 ± 1.1</td>
<td>11.0 ± 1.3</td>
<td>9.7 ± 0.9</td>
</tr>
<tr>
<td>( \text{PCH}_3 )</td>
<td>8.1 ± 1.1</td>
<td>7.9 ± 0.9</td>
<td>7.0 ± 0.8</td>
<td>8.2 ± 1.1</td>
</tr>
<tr>
<td>( \text{AsCH}_3 )</td>
<td>6.7 ± 2.1</td>
<td>6.6 ± 2.3</td>
<td>6.1 ± 2.7</td>
<td>9.6 ± 1.5</td>
</tr>
<tr>
<td><strong>Group VI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \text{O} )</td>
<td>14.4 ± 2.8</td>
<td>13.8 ± 0.7</td>
<td>14.5 ± 0.7</td>
<td></td>
</tr>
<tr>
<td>( \text{S} )</td>
<td>8.6 ± 0.8</td>
<td>9.1 ± 1.3</td>
<td>9.0 ± 1.0</td>
<td></td>
</tr>
<tr>
<td>( \text{Se} )</td>
<td>7.1 ± 0.9</td>
<td>7.7 ± 0.8</td>
<td>7.6 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>( \text{Te} )</td>
<td>4.2 ± 0.5</td>
<td>4.5 ± 0.6</td>
<td>4.4 ± 0.7</td>
<td></td>
</tr>
</tbody>
</table>

* From Lambert and Netzel. 17

![Fig. 23. \(^{139}\text{La} \) spin-lattice relaxation rate as a function of the molar concentration of added \( \text{NaCl} \), \( \text{LiClO}_4 \), and \( \text{LiNO}_3 \). (From Reuben. 46)](image-url)
overall tumbling rate of the molecule.\(^9\) Segmental motion has been observed in the long alkyl chains of 1-decanol\(^{86, 87}\), lecithin,\(^{88}\) aliphatic amides,\(^{77}\) and oximes.\(^{77}\)

Table III lists the \(^{13}\)C relaxation times for the various substituted butanes. From the relaxation data in Table III, the overall tumbling rate for both \(n\)-BuNH\(_2\) and \(n\)-BuONO is greater than those for the other compounds as indicated by the longer relaxation times. Molecular association accounts for the short relaxation times for \(n\)-BuNH\(_2\) and the large molecular size of \((n\text{-Bu})_2\text{NCOH}\) accounts for its short relaxation times. Variation of the relaxation time along the alkyl chain in these compounds is the result of segmental motion.

4. Molecular Diffusion. An important aspect of the spin-echo technique is that it can be employed to determine the coefficient of self-diffusion,\(^{19, 90}\) which is an important parameter in the understanding of microdynamic structures of liquids, polymers, and solids having internal degrees of motion.

Self-diffusion coefficients are determined using a time-dependent field gradient technique,\(^{92}\) which is a modification of the spin-echo technique described in Section IID. The modification involves the gating of the magnetic field gradient. The attenuation factor, \(R\), of the echo amplitude resulting from the field gradient technique is given by the following expression:\(^{92}\)

\[
\ln R = -\gamma^2 g^2 \delta^2 \left( \Delta - \frac{1}{3} \delta \right) D
\]

where \(\gamma\) is the gyromagnetic ratio of the nuclei being investigated, \(D\) is the diffusion coefficient, \(\delta\) is the width of the gradient pulses, \(\Delta\) is the separation of gradient pulses, and \(g\) is the amplitude of the time-dependent pulsed gradient.

This technique has been used to measure diffusion in colloidal systems.\(^{14, 92}\) The colloidal structure can restrict the diffusional motion\(^{93, 94}\) and when the colloidal structure is of the same order of magnitude as the diffusion distance, the maximum effect will be observed.

A plot of \(\ln R\) vs \(g^2 \delta^2 (\Delta - 1/3 \delta)\) will be a straight line for a single species in a homogeneous phase. A single curve line will result if several noninteracting species are observed simultaneously. If restricted diffusion is operating, \(\ln R\) will be a function of the two variables \((g\delta)^2\) and \((\Delta - 1/3 \delta)\) instead of the single variable \(g^2 \delta^2\) \((\Delta - 1/3 \delta)\).

Fig. 24 shows the effects of varying the parameter \(g^2 \delta^2\) for two values of the parameter \((\Delta - 1/3 \delta)\) in the investigation of diffusion within living cells of tobacco pith.\(^{95}\) Since two separated curves are observed, restricted diffusion within the living cells is indicated.

5. Adsorption. Because motional properties of molecules are revealed through relaxation studies of the nuclear spin system, relaxation spectroscopy can therefore be useful in characterizing motional behavior of molecules adsorbed on solid surfaces.\(^{85-97}\) In general, the spin-echo techniques are used to determine both \(T_1\) and \(T_2\) as well as the diffusion coefficients for adsorbed molecules. These parameters are determined as a function of the surface coverage, temperature, and different frequencies of the nucleus of interest. Relaxation times of adsorbed molecules are generally shorter than those in the bulk liquid due to restricted molecular mobility in the adsorption layer arising from various types of intermolecular interactions. A study of the adsorption of benzene on modified silica surfaces\(^{98}\) will illustrate the type of information that can be obtained from NMR relaxation measurements.

The amount of benzene adsorbed on hydroxylated and methylated silica was determined from the spin-echo amplitude extrapolated to zero time (see Section III B). Figs. 25 and 26 show the relationships between the amount of adsorbed benzene on the two silica samples and the relaxation times \(T_1\) and \(T_2\), respectively. Both

### Table III. Segmental motion in various substituted butanes.

<table>
<thead>
<tr>
<th>Compound</th>
<th>(^{13})C spin-lattice relaxation times for carbon atoms (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\delta)-CH(_3)</td>
</tr>
<tr>
<td>(n)-BuNH(_2)</td>
<td>3.35</td>
</tr>
<tr>
<td>((n\text{-Bu})_2\text{NCOH})</td>
<td>3.1</td>
</tr>
<tr>
<td>(n)-BuOH</td>
<td>6.0</td>
</tr>
<tr>
<td>(n)-BuONO</td>
<td>9.5</td>
</tr>
<tr>
<td>(n)-BuNH(_2)</td>
<td>12.1</td>
</tr>
</tbody>
</table>
$T_1$ and $T_2$ were found to be exponential over the whole range of surface coverage measured, thus indicating a one-phase relaxation system that results from a rapid exchange of molecules among different relaxation environments. From the data shown in Fig. 25 it can be concluded that the adsorbed benzene molecules are more strongly bound to the hydroxylated than to the methylated surface. The strong intermolecular interaction of the benzene molecule with the hydroxylated surface is due to hydrogen bonding of the $\pi$-electrons with the surface OH groups. Fig. 26 shows that the $T_2$ values for adsorbed benzene on hydroxylated and methylated surfaces are nearly the same. Thus the OH group cannot be responsible for the effect. Since the surface OH groups are not involved, the strong adsorption site is due to overlapping potential fields.

The spin-lattice and spin-spin relaxation times for benzene at room temperature are equal (19 s). For adsorbed benzene $T_1$ was found to be shorter by a factor of 10 and $T_2$ was reduced by a factor of greater than 1000. It was concluded that $T_1$ and $T_2$ are each determined by molecules adsorbed on different regions of the surface. Molecules adsorbed on weaker adsorption sites and in higher layers give rise to $T_1$, while $T_2$ arises primarily from molecules adsorbed on strong adsorption sites.

Both $T_1$ and $T_2$ increase with increasing surface coverage. This effect arises from the "dilution" of the initial adsorbed molecules having short relaxation times with molecules having longer relaxation times as a result of being in a weaker site and in higher layers.

Fig. 27 shows the relationship between the diffusion coefficient for benzene and the surface coverage for the hydroxylated and methylated surfaces. A significant difference between the two surfaces is observed at low surface coverages. Within the range below the monolayer coverage (indicated by an arrow), the diffusion coefficient for benzene on the methylated surface decreases with increased surface coverage as a result of hindrance of the adsorbed molecules with increased density of the adsorption layer. The diffusion coefficient, however, increases with increased surface coverage for benzene adsorbed on the hydroxylated surface because of the increased interaction between the $\pi$-electron of the benzene molecules with more surface OH groups.

B. Analytical Applications. A number of analytical applications based upon the nuclear relaxation phenomena of nuclei have appeared in the literature. These methods generally used the initial amplitude or some intermediate amplitude of the FID resulting from a 90° pulse or spin echo pulse sequence. The magnetization function $M_0 - M_t$ as determined by the inversion-recovery technique at time equal to zero has also been used in quantitative analysis. The following sections describe briefly how the relaxation properties of nuclei can be used to obtain analytical information about a material.

1. Basic Analytical Equations. In a frequency domain spectrum the area under a resonance signal is related to the spin concentration for that particular nuclear spin. The same information is contained in the time domain spectrum (FID). Proof that this is so can be obtained from the Fourier transformation equations relating the frequency domain spectrum to its time domain spectrum. The equations are:

$$g(\omega) = \int_{-\infty}^{\infty} f(t) e^{-i\omega t} dt$$

$$f(t) = \int_{-\infty}^{\infty} g(\omega) e^{i\omega t} d\omega$$

where $g(\omega)$ and $f(t)$ are the signal amplitude in the frequency domain and time domain spectrum, respectively, $\omega$ is the resonance frequency of the nuclei of interest, and $t$ is the time.

Focusing attention on Eq. (30), letting $t = 0$, and evaluating the transform yields:

$$f(0) = \int_{-\infty}^{\infty} g(\omega) d\omega$$

The right side of Eq. (31) is just the definition of the area under a spectral line, whereas the left side is the FID amplitude at zero time. The important feature of Eq. (31) is that the initial amplitude measurement in the time domain is equivalent to the total area measurement in the frequency domain. Thus, either measure-
ment can be used to perform quantitative analyses. If only one resonance signal exists in the sample, the FID will generally decay exponentially. For solids, however, there is no reason to assume exponential free induction decay. 8

The initial amplitude of the FID will be related to the sum of the spin concentrations if more than one resonance signal is present as a result of differences in the chemical shifts or coexistence of two phases within the sample. Many of the quantitative applications of pulsed NMR utilize the fact that nuclei in different phases relax at different rates when perturbed by an rf pulse. The resulting FID is then the sum of two or more exponential decays.

Fig. 28 represents a composite FID resulting from nuclei in two distinct environments. The short and long relaxation times correspond to solids and liquid phases, respectively. Liquids have long \( T_2 \) values and relax more slowly than solids after the rf pulse, because the molecular motion that occurs in liquids causes the dipole-dipole interactions to be inefficient relative to dipolar interactions in solids. For nonviscous liquids in a homogeneous field, the slowly relaxing components in the free induction decay are of the order of seconds. As the liquid becomes more viscous, or is cooled, the relaxation times become shorter because of the restricted mobility in such systems. Typically these occur in the millisecond range. Finally in solids, when the nuclei are in a more rigid environment, dipole-dipole interactions are very efficient and relaxation times for solids are very short (microsecond range).

The amplitude of a FID resulting from a two-phase system with each component decaying exponentially can be expressed as follows:

\[
M_t = M_0^s e^{-t/T_2^s} + M_0^l e^{-t/T_2^l}
\]  

(32)

where \( M_0^s \) and \( M_0^l \) are the equilibrium concentrations of nuclei having the short and long relaxation times, \( T_2^s \) and \( T_2^l \), respectively, and \( M_t \) is the total FID amplitude at any given time, \( t \).

From a semilog plot of \( M_t \) vs \( t \), values of \( M_0^s \), \( M_0^l \), and \( M_t \) can be obtained by graphical extrapolation (at \( t = 0 \), \( M_t = M_0^s + M_0^l \)). The value of \( M_0^s \) can be obtained by extrapolation of the long time portion of the FID to zero time. The value of \( M_0^s \) is obtained from the difference \( M_0^s - M_0^l \). For multicomponent systems the Weibull function has been used to resolve the complex FID curves. 9, 10

2. Polymer Research. Free induction decays from polymers, having a certain degree of crystallinity, generally are composed of two components—one due to the crystalline phase, the other to the amorphous phase. The \( T_2 \) from the amorphous phase is longer than its crystalline counterpart, and is generally exponential. The shape of the FID resulting from relaxation in the crystalline phase in nonexponential.

The accuracy of pulsed NMR to determine the degree of crystallinity depends upon the relaxation times, \( T_2 \), of each phase, upon how well the \( T_2 \) values can be resolved, and upon the types of molecular motion occurring in the system. For linear polyethylene the NMR results agree well with x-ray and specific volume measurements, but not for branched polyethylene, since the crystalline phase is markedly temperature dependent. 101, 102 One reason for the poor agreement is that the NMR relaxation measurements reflect the motions occurring in the system, and the crystalline phase is one of order. The ratios of long and short relaxation components in polymers reflect a “rigidity” ratio that can be used to provide useful information about molecular motion. 103 NMR measurements based on the relaxation properties of polymers have been used to calculate the relative contributions of the crystalline and amorphous phases in polymers that were then used to determine polymer densities. 104 Similar NMR measurements of the "hard" and "soft" segments of block copolymeric thermoplastic elastomers have provided useful information about the physical properties of such systems. 105

The hardening process of a polymer solution can be monitored by determining the solid/liquid ratio. This ratio can be determined from the amplitude of the function \( M_0 - M_t \) at \( t = 0 \) for the solid-liquid mixture and extrapolation of the function for the solid phase free of liquid polymer (Fig. 29). 106 The percent solid in the polymer solution (48.3%) can be calculated from Eq. (33):

\[
\% \text{solid} = \frac{(M_0 - M_t)_0}{(M_0 - M_t)_{100}} \times 100
\]  

(33)

3. Agricultural and Food Research. An analytical pulse NMR method to determine the oil content of living seeds 105 that is nondestructive and rapid when com-

![Fig. 28. An illustration of the FID for a two-component system, each component having a different exponential relaxation rate.](image)

![Fig. 29. Spin amplitude function \((M_s - M_t)\) vs the pulse spacing for a polymer solution containing both solid and liquid phases. (From Bruker Instruments, Inc.)](image)
pared to chemical methods has been developed. The
method provides a means for selecting seeds that will
yield a crop containing a high percentage of oil (Fig.
30). The amplitude of the free induction decay after a
90° pulse is measured at a time sufficiently long so that
the signals due to protons in bound water, carbohydrates,
and proteins (non-oil matrix) make no contribution.
Their $T_2$ values are short and have attained their
equilibrium value of zero. The hydrogens of the oil
content, however, being more mobile, have longer $T_2$
values.

The oil contents of the seeds were determined from a
calibration curve prepared from the FID amplitude at a
given time for seeds of known oil content. Comparison
tests between the NMR, Soxhlet extraction, and steel
tube methods, on 60 Brassica seed samples showed that
better reproducibility was achieved using the NMR
method. Reproducibility was on the order of ±1%.
Recently, $^{13}$C measurements employing sophisticated
pulsed NMR techniques have been used in the selection
of seeds for breeding.

Magnetic resonance measurements have found many
useful applications in the food processing industry.
A standard analytical method for the measurement of
solid/liquid ratios in fats is under consideration. The
method relies on differences in relaxation times be-
tween protons in solid and liquid fats. The
agreement between pulsed NMR determination of solid fat
content and the more laborious dilatometric measure-
ments was excellent for 48 fats and fat mixtures. Regression analyses between the two measurements
yielded a standard deviation of 1.8% over the effective
range of 0 to 90% solids in fats. The pulsed NMR meas-
urements required about 6 s to obtain a standard devia-
tion of 0.3% for the solid content in fats.

4. Petroleum Research. Relaxation measurements
have been applied to analytical problems in fossil en-
ergy research. Spin-spin relaxation times for protons
in oil shale are shorter than the $T_2$ values for protons in
the mineral rock containing both free and adsorbed
water. FID measurements on samples of illite show that
the $T_2$ value is about 50 µs, whereas the $T_2$ value for the
organic material in oil shales is about 15 µs.

Fig. 31 shows the FID spectra resulting from oil shale
heated to remove free water. For situations in which
adsorbed water might contribute to the NMR signal,
two measurements were made, one immediately after
the pulse (20 µs) and one along the FID where the
organic hydrogen signal had decayed nearly to zero (50
µs). The signal remaining was attributed to adsorbed
water in clay minerals, and was subtracted from the
total signal to yield a measurement proportional to the
organic hydrogen content of oil shales from which the oil
yield could be calculated. The yields calculated from the
FID amplitudes for oil shales have been found to corre-
late linearly with the Fischer assay oil yield (Fig. 32).

A rather unique application of relaxation spectroscopy
is the nuclear magnetism log (NML). This device
detects the free precession of protons in the earth's
magnetic field. First, a polarizing field much stronger
than the earth's is generated by passing current
through a coil in the logging sonde. The induced mag-
netization grows exponentially with time at a rate de-
termined by the $T_1$ of the fluids in the formation. The
magnitude depends upon how long the current flows.
Typically a few seconds is necessary to establish an equilibrium magnetization in a direction different from the field direction of the earth's magnetism. When the current is turned off, the polarizing field collapses and the protons are free to precess in the earth's magnetic field. This free precession gives rise to a FID, whose amplitude is proportional to the amount of fluid in the formation pores. The uniqueness of the NML technique compared to other well logging methods is that its signal arises solely from the free fluid in the pores. The NML response is reported as the free fluid index. Porosities, permeabilities, and residual oil in petroleum formations and reservoirs also have been deduced from NML data.

5. Medical Research. Nuclear spin relaxation spectroscopy has also been applied to areas of cellular biology and cancer research. Typically these studies concern themselves with the physical state of water and ions inside living cells, and the freedom of movement of intra- and extracellular water molecules. Whether intracellular water possesses properties of bulk water, i.e., free water, or is highly structured, i.e., "icelike," is an active area of NMR investigations. Similarly the degree of motional freedom of water molecules in normal and cancerous tissues results in measurable differences in spin-lattice relaxation times of water in these tissues (Fig. 33). Generally, cancerous tissues yield longer spin-lattice relaxation times than do normal tissues. The hope is that these differences may be exploited as a diagnostic tool in cancer research.

IV. CONCLUSIONS

It is evident from the text that whenever changes in motion of molecules are involved, nuclear spin relaxation spectroscopy can be an important technique to probe the molecular dynamics. Nuclear spin relaxation techniques have been used in many applications that were not discussed in this article. One such application of the relaxation phenomena is in the investigation of chemical exchange of molecular species. Not discussed but of significance is the relaxation phenomena as it relates to the theory of metals and metal alloys. For details of the nuclear spin relaxation in solid and gases the reader is referred to reviews by and Govil, respectively.

From relaxation data, instrumental parameters can be adjusted properly for quantitative analysis, solvent signals may be suppressed to reveal hidden resonance signals, and relaxation times may be altered by using relaxation reagents in an effort to obtain rapidly NMR spectra of dilute samples having long relaxation times.

The uses of nuclear spin relaxation spectroscopy will continue to expand as the instrumentation to investigate relaxation behavior of $^{13}$C, $^{15}$N, and less familiar nuclei becomes more accessible. As the theory for describing anisotropic motion of molecules becomes more fully developed, the motions and physicochemical behavior of larger and more complex molecules will also be investigated.

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64. E. L. Hahn, Phys. Rev. 80, 580 (1950).
The Application of Fourier Transform Spectroscopy to the Remote Identification of Solids in the Solar System

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The techniques of Fourier transform spectroscopy combined with large aperture telescopes and advances in detector technology now permit infrared (\(\lambda > 1 \mu\)) observations of the surfaces of small solar system objects such as asteroids and satellites. The results demonstrate that this activity can produce important new compositional information related to the origin and evolution of the solar system. The detection of water ice in Saturn's rings and on some of the satellites of Jupiter and Saturn confirm expectations that ices are important mineralogical components in the chemistry of the outer solar system. More recent studies of the mineralogical composition of the surfaces of asteroids provide a new observational link to the origin of meteorites and the early thermal history of the solar system. These results have been dependent upon supporting laboratory studies of the spectral behavior of ices and minerals to define the potential, and limitations, of the method. Since many of the astronomical observations have been exploratory in nature, prospects are good that continued refinement of the techniques will lead to additional insights.

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Index Headings: Fourier transform spectroscopy; Infrared astronomy; Planetary surfaces.

INTRODUCTION

Basic questions concerning the origin and evolution of our solar system frequently depend upon compositional information. Observational data contributing to this knowledge include determinations of densities, which impose important constraints on composition, and detailed laboratory analyses of extraterrestrial samples systematically procured in the space program or capriciously provided by nature as meteorites. Among techniques for determining compositions through remote analysis, the use of spectroscopy at ground-based telescopes is certainly the most important. During the past decade sophisticated engineering designs and advances in computer and detector technologies have been incorporated into the classical Michelson interferometer to produce the Fourier transform spectrometer (FTS). The use of these instruments for solar system studies is commonly associated with studies of atmospheres. This has been a very productive endeavor since the near-infrared spectra of most gases are characterized by prominent vibration-rotation bands which under moderate to high spectral resolution reveal structure highly diagnostic of individual molecular species and the physical conditions (pressure, temperature) under which they are observed. The solar system also contains many smaller bodies devoid of atmospheres, such as the asteroids and satellites, whose physical properties must also be determined for a more complete understanding of our solar system. A systematic study of the surfaces of these objects with remote sensing techniques such as infrared Fourier spectroscopy can produce new data concerning the chemistry of the primordial solar nebula, the origin of meteorites, and the collisional and thermal history of the early solar system. In spite of this promise, however, historically the spectral study of solids in the solar system with infrared techniques has progressed slowly. The objects under consideration are quite faint so that spectral data were difficult to obtain for even the brightest of them. Also, compared to gases the spectra of most solids are very much less informative. Interpretation is primarily limited to empirical comparisons employing none of the mathematical formalism of spectral line formation frequently used in analyses of gaseous spectra. Nevertheless, remote mineralogical sensing is an emerging, interdisciplinary field of planetary science spurred by new observational opportunities, analyses of lunar rocks and meteorites, and laboratory spectral studies of terrestrial minerals and ices. In this review we limit ourselves to the role of infrared spectroscopy in these studies from 1 to 2.5 \(\mu\) by means of FTS. We begin with a brief description of the astronomical objects themselves and the instrumen-