

5 Nuclear Magnetic Resonance Spectroscopy

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1 Introduction

The multitudinous aspects of n.m.r. spectroscopy render it impossible for a report of this size to cover all of them adequately and justly. Thus, it has been decided to concentrate on the advances that have been made during the past two years in areas of continuing or growing importance to physical chemists and chemical physicists.

The report is organized by means of phenomenon rather than application, providing an illustrative covering for each section considered together with some key references. The examples chosen usually provide ready access to related work. For a more detailed coverage the reader is referred to the Specialist Periodical Reports on N.M.R.,¹ which also contain comprehensive lists of books and reviews.

In recent years developments in multinuclear instrumentation, multiple resonance techniques, and high resolution n.m.r. spectra from solid samples have served to turn attention away from the routine compilation of solution chemical shift and spin coupling data for nuclei such as ^1H , ^{13}C , ^{19}F , and ^{31}P . Most elements of the periodic table have at least one n.m.r. nuclide and a majority of these have now received some spectroscopic attention.² Some of the examples mentioned in this report are chosen to reflect this development. The recent rapid growth of interest in the n.m.r. of the more difficult nuclei is expected to continue, in line with the expanding availability of higher magnetic fields and multiple resonance facilities.

The present growth rate in publications dealing with high-resolution spectra of solid samples serves to indicate that this area of n.m.r. is heading for a boom period. It is hoped that this report provides a flavour of the recent advances in the major growth areas of n.m.r. as well as mentioning some of those in the more traditional n.m.r. studies and developments in the theoretical understanding of n.m.r. parameters.

2 Multiple Magnetic Resonance

Traditionally, a multiple resonance experiment has been one in which several r.f. fields

¹ 'Nuclear Magnetic Resonance', ed. G. A. Webb (Specialist Periodical Reports), The Royal Society of Chemistry, London, 1980, Vol. 9; 1981, Vol. 10.

² 'NMR and the Periodic Table', ed. R. K. Harris and B. E. Mann, Academic Press, London, 1978.

are applied simultaneously to the sample.³ A more satisfactory definition for modern experimental techniques is 'one in which the spin system is affected by several r.f. fields'.

In recent years the major expansions in this area have occurred in the uses of two-dimensional n.m.r. spectroscopy, selective excitation, the interproton and ^{13}C - $\{^1\text{H}\}$ nuclear Overhauser effects (NOE), and high-resolution spin-echo experiments.

Two-dimensional N.M.R.—Two very readable reviews of two-dimensional Fourier transformation (FT) experiments in high-resolution n.m.r. have been published.^{4,5} Both the theoretical and experimental aspects of the subject are covered.

At present there are three main areas of applications of two-dimensional n.m.r. The first involves the separation of n.m.r. parameters in the two frequency dimensions, *e.g.*, chemical shifts in one dimension and multiplet structure in the other. Another application relates to the correlation of n.m.r. parameters, *e.g.*, the correlation of heteronuclear chemical shifts. The third application deals with the observation of normally forbidden transitions. This has given rise to a number of multiple quantum experiments. All of these fields of application have received attention and have continued to expand in the period under review.

An example of a chemical-shift correlation map for the protons and ^{13}C nuclei of the aliphatic region of 2-(1-methylcyclohexyl)-4,6-dimethylphenol is presented in Figure 1.⁶ This molecular 'fingerprint' allows a more direct measurement of the frequencies concerned than would a more traditional multiple trace display. The pulse sequence used to obtain this map is given in Figure 2, where Δ_1 and Δ_2 are delays designed to avoid signal cancellation. The 180° refocusing pulse is applied to the ^{13}C nuclei at the centre of the evolution period, t_1 , to remove the large one-bond couplings in the proton dimension. The same coupling is eliminated in the ^{13}C dimension by noise decoupling applied during the free induction decay (FID). This is one of a number of procedures that can be employed to obtain correlation maps.⁷

Most applications of heteronuclear two-dimensional n.m.r. are concerned with chemical-shift correlations. However, the same technique provides a unique procedure for the indirect measurement of proton-proton couplings.⁸⁻¹⁰ This can be usefully employed in the analysis of complex spin systems where the normal spectrum is very crowded or covered by signals from solvent or impurity molecules. Applications in spectral analysis include those for the 1', 2', and 5' protons in the ribose ring of 2'-guanosine monophosphate¹¹ and for the proton spectrum of 2',3'-cyclic uridine monophosphate.⁹ In the latter case the protons are coupled to more than one phosphorus nucleus, which causes the appearance of the spectra to be flip-angle

³ R. A. Hoffman and S. Forsén, in 'Progress in NMR Spectroscopy', ed. J. Emsley, J. Feeney, and L. H. Sutcliffe, Pergamon, London, 1966, Vol. 1, p. 15.

⁴ W. McFarlane and D. S. Rycroft, in 'Annual Reports on NMR Spectroscopy', ed. G. A. Webb, Academic Press, London, 1979, Vol. 9, p. 319.

⁵ R. Freeman and G. A. Morris, *Bull. Magn. Reson.*, 1979, **1**, 5.

⁶ R. Freeman and G. A. Morris, *J. Chem. Soc., Chem. Commun.*, 1978, 684.

⁷ P. Bachman, W. P. Aue, L. Müller, and R. R. Ernst, *J. Magn. Reson.*, 1977, **28**, 29.

⁸ P. H. Bolton and G. Bodenhausen, *J. Am. Chem. Soc.*, 1979, **101**, 1080.

⁹ G. Bodenhausen and P. H. Bolton, *J. Magn. Reson.*, 1980, **39**, 399.

¹⁰ G. Bodenhausen, *J. Magn. Reson.*, 1980, **39**, 175.

¹¹ L. Müller, *J. Am. Chem. Soc.*, 1979, **101**, 4481.

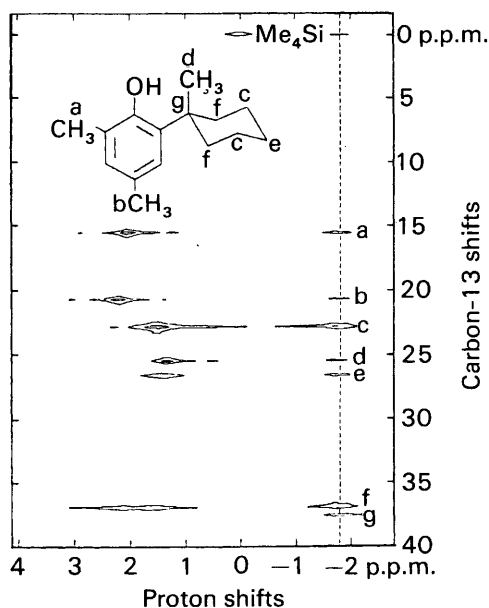


Figure 1 Chemical shift correlation map of the aliphatic resonances of 2-(1-methylcyclohexyl)-4,6-dimethylphenol showing contours of equal intensity. TMS acts as the reference point for both frequency dimensions

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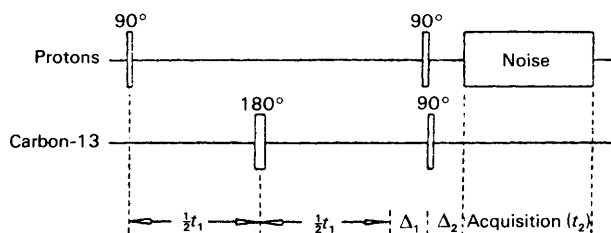


Figure 2 Pulse sequence used for obtaining chemical shift correlation maps

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dependent. This unwanted effect is removed by taking the appropriate combination of spectra.

Although most heteronuclear two-dimensional experiments involve the correlation of single quantum transitions for the two nuclear species, it is also possible to produce a correlation with forbidden heteronuclear multiple quantum transitions. In this way the single quantum transitions of the second species are obtained. This approach has been considered in the case of ^{13}C enriched methyl iodide and the ^{13}C spectrum has been obtained with full proton sensitivity.¹¹

The measurement of relaxation times of spins whose resonances suffer serious

overlapping is another application of two-dimensional n.m.r.¹² This is achieved by transferring features of the relaxation behaviour of the desired nucleus to another, unobserved, resonance. The same technique may be used to study heteronuclear cross relaxation.

To obtain a correlation of chemical shifts with couplings in heteronuclear experiments it is usual to employ full decoupling during one time period and none during the other. However, by means of off-resonance decoupling the chemical shift axis contains splittings due to the couplings that are scaled by the degree of off-set from resonance in the proton spectrum. This provides an additional parameter for the analysis of complex spectra.¹³

The detection of forbidden multiple quantum transitions by means of multiple pulse sequences¹⁴ may be used to determine molecular motion. An application of this technique is provided by the two-dimensional deuterium spectrum¹⁵ of a liquid crystalline solution of $\text{DC}\equiv\text{C}-\text{C}\equiv\text{N}$. The accurate measurement of the double quantum transition provides information on the Redfield relaxation elements.

Two-dimensional spectra of systems exhibiting chemical exchange may be obtained by the pulse sequence given in Figure 3.¹⁶ The *modus operandi* in this case is that the

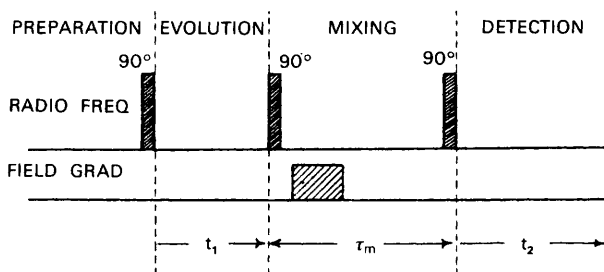


Figure 3 Experimental scheme for two-dimensional exchange spectroscopy (Reproduced by permission from *J. Am. Chem. Soc.*, 1979, **101**, 6442)

magnetization components are labelled with their precessional frequencies during the evolution period. Thus, after exchange, it is possible to determine their origin and trace out the exchange pathways. The purpose of the magnetic field gradient pulse is to destroy transverse interference between the evolution and detection periods. Optimization of the mixing time and of other parameters has been considered as well as the possible effects of different exchange rates.¹⁷

The chemical exchange network of the heptamethylbenzenonium ion (1) has been elucidated by this technique.

¹² A. G. Avent and R. Freeman, *J. Magn. Reson.*, 1980, **39**, 169.

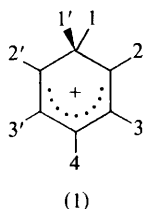
¹³ L. Müller, *J. Magn. Reson.*, 1980, **38**, 79.

¹⁴ A. Wokaun and R. R. Ernst, *Chem. Phys. Lett.*, 1977, **52**, 407.

¹⁵ G. Bodenhausen, N. M. Szeverenyi, R. L. Vold, and R. R. Vold, *J. Am. Chem. Soc.*, 1978, **100**, 6265.

¹⁶ B. H. Meier and R. R. Ernst, *J. Am. Chem. Soc.*, 1979, **101**, 6441.

¹⁷ J. Jeener, B. H. Meier, P. Bachmann, and R. R. Ernst, *J. Chem. Phys.*, 1979, **71**, 4546.



The two-dimensional proton contour plot is given in Figure 4, from which it is apparent that the four non-equivalent methyl groups (1,1', 3,3', 2,2', and 4) are present on the main diagonal with the appropriate intensity ratio of 2:2:2:1. The presence of

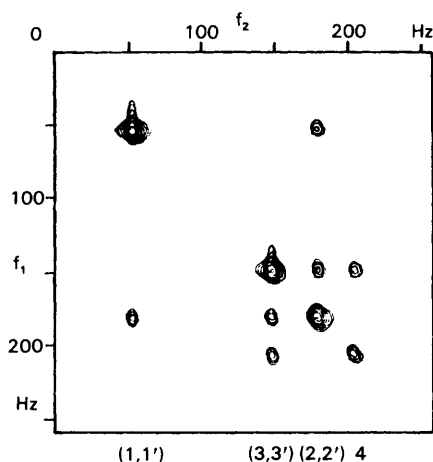


Figure 4 Contour plot of the two-dimensional ^1H exchange spectrum of heptamethylbenzenonium ion in 9.4 M H_2SO_4 obtained by a two-dimensional Fourier transformation from 64 free induction decays with t_1 values ranging from 0 to 142 ms and with $\tau_m = 280$ ms

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the off-diagonal peaks indicates exchange occurring between the two methyl groups connected by a given off-diagonal peak. The cross peaks between the 1 and 2, 2 and 3, and 3 and 4 methyls indicate a $1 = 2 = 3 = 4$ exchange network that is consistent with a 1–2 shift mechanism.¹⁶

Selective homonuclear decoupling in two-dimensional J resolved spectroscopy has been thoroughly investigated.¹⁸ This technique has a number of applications including the simplification of complex spectra, the identification of pairs of coupled nuclei, and phase separation to give pure absorption spectra.¹⁸ By using a second pulse of 90° rather than 180° in a homonuclear two-dimensional J spectrum more detailed information may be obtained on the relationship of the coupled nuclei. Homonuclear

¹⁸ K. Nagayama, *J. Chem. Phys.*, 1979, **71**, 4404.

two-dimensional J spectroscopy can also be employed as an alternative to broad-band heteronuclear and homonuclear decoupling.¹⁹

In principle two-dimensional homonuclear correlated spectra can be used to elucidate the connectivity between coupled nuclei. However, even for medium sized molecules, this technique has not been extensively employed owing to the requirement of a very large data set. Recently, two experimental procedures have been reported²⁰ that are suitable for handling the large data matrices encountered in work on macromolecules. These are known by the intriguing acronyms SECSY and FOCYSY. The former of which stands for spin-echo correlated spectroscopy and the latter for fold-over correlated spectroscopy. It seems very probable that these two techniques will become valuable tools in the elucidation of complex high-resolution n.m.r. spectra of large molecules.

Selective Excitation and Detection.—For small molecules selective excitation appears to be superior to two-dimensional n.m.r. techniques. However, for large molecules selective excitation tends, at present, to be too time consuming to be of practical utility.

The DANTE pulse sequence yields high resolution proton-coupled spectra of single carbons and has thus found application in conformational analysis.^{21,22} A further use of DANTE has been in the identification of homonuclear ^{13}C couplings.²³

The transfer of coherence to non-irradiated, possibly forbidden, transitions by selective excitation in a spin-spin multiplet has been successfully applied in AX, AX₂, and AX₃ heteronuclear spin systems.²⁴

Selective ^{13}C excitation allied with gated proton decoupling permits the accurate determination of ^{13}C – ^1H couplings.²⁵ In conjunction with single frequency off-resonance decouplings, J scaling is achieved. The poor signal-to-noise ratio (S/N) produced by this procedure can be avoided by applying a 'mask' consisting of multiplying the FID by a weighting function that is matched to the required part of the spectrum.

The main interest in J scaling arises from the possible occurrence of intensity anomalies in off-resonance ^{13}C – $\{^1\text{H}\}$ spectra under poor S/N conditions, which can lead to serious interpretation problems. By means of computer simulation it has been demonstrated that the main cause of these anomalies is spatial inhomogeneity of the decoupling r.f. field.²⁶

A practical guide to the use of multiple pulse scaling techniques in ^{13}C – $\{^1\text{H}\}$ n.m.r. has appeared.²⁷ Data are provided that allow the optimization of the various experimental factors controlling the degree of scaling.

J cross polarization (JCP) refers to the transfer of spin magnetization between two nuclei by means of scalar coupling. The main advantages of a JCP experiment over conventional FT n.m.r. in the case of a ^{13}C – $\{^1\text{H}\}$ situation are that (i) the pulse

¹⁹ L. D. Hall and S. Sukumar, *J. Am. Chem. Soc.*, 1979, **101**, 3120.

²⁰ K. Nagayama, A. Kumar, K. Wüthrich, and R. R. Ernst, *J. Magn. Reson.*, 1980, **40**, 321.

²¹ G. A. Morris and R. Freeman, *J. Magn. Reson.*, 1978, **29**, 433.

²² G. A. Morris and R. Freeman, *J. Am. Chem. Soc.*, 1978, **100**, 6763.

²³ A. A. Chalmers, *J. Magn. Reson.*, 1980, **38**, 565.

²⁴ P. M. Henrichs and J. Schwartz, *J. Chem. Phys.*, 1978, **69**, 622.

²⁵ G. E. Martin, *J. Heterocycl. Chem.*, 1978, **15**, 1539.

²⁶ R. Freeman, J. B. Grutzner, G. A. Morris, and D. L. Turner, *J. Am. Chem. Soc.*, 1978, **100**, 5637.

²⁷ W. P. Aue, D. P. Burum, and R. R. Ernst, *J. Magn. Reson.*, 1980, **38**, 375.

repetition rate is governed by $T_1(^1\text{H})$, which is normally shorter than $T_1(^{13}\text{C})$, and (ii) the ratio $\gamma(^1\text{H}):\gamma(^{13}\text{C})$ should lead to a four-fold ^{13}C intensity enhancement. The JCP method has been applied to some natural abundance ^{15}N spectra of compounds with reasonably large ^{15}N – ^1H scalar couplings²⁸ and to the ^{29}Si spectra of some molecules with large couplings.²⁹

An experimental difficulty associated with JCP is the high precision required in meeting the Hartmann–Hahn condition. A somewhat less instrumentally demanding technique is INEPT, which stands for insensitive nuclei enhanced by polarization transfer.³⁰ A signal enhancement twice as great as that expected from the NOE is normally obtained from INEPT, thus making it especially useful for nuclei having a negative magnetogyric ratio.

The dramatic improvement produced by INEPT and proton decoupling in the ^{15}N spectrum of benzyloxycarbonylglycylglycine methyl ester provides an example of the utility of INEPT.³¹ The overall sensitivity of this experiment is controlled by the low ^{15}N measuring frequency. Improvement is achieved by means of a ten-pulse sequence, which transfers magnetization from protons to ^{15}N and then, after probing the ^{15}N screening, returns the magnetization to the protons in order to utilize their higher detection sensitivity. The resulting display can be a two-dimensional spectrum in which the nitrogen and proton dispersions are presented along the two axes. High S/N spectra have been obtained by this procedure for *N*-acetylvaline containing ^{15}N in natural abundance.³²

An equivalent result to that found by the INEPT sequence with proton decoupling may be obtained by a sequence of selective population transfers involving both sets of spins.³³ However, since this procedure depends upon chemical shifts it is not as generally useful as the INEPT scheme.

Phase anomalies for different multiplet components may arise in JCP experiments without proton decoupling. Consequently the accurate determination of couplings may be difficult. Such problems are removed in the PCJCP (phase-corrected JCP) scheme, whereby the spin locking field remains active for an additional amount of time dependent upon the value of B_1 .³⁴

The sensitivity of JCP experiments to the exactness of the Hartmann–Hahn match and the size of the scalar coupling is reduced by means of a refocusing procedure (RJCP).³⁵ The RJCP procedure can cope with a mismatch of the Hartmann–Hahn condition of about ± 0.2 db without significant intensity loss.

Another way of removing the difficulty of obtaining a Hartmann–Hahn match is by simultaneously varying the amplitudes of the r.f. fields for the coupled nuclei in the opposite sense. When cross-over occurs there is a match and a corresponding adiabatic transfer of magnetization (AJCP). This technique has been demonstrated to give an excellent S/N for the ^{15}N spectra of a mixture of amides.³⁶

²⁸ R. D. Bertrand, W. B. Moniz, A. N. Garraway, and G. C. Chingas, *J. Magn. Reson.*, 1978, **32**, 465.

²⁹ P. D. Murphy, T. Taki, T. Sogabe, R. M. Metzler, T. G. Squires, and B. C. Gerstein, *J. Am. Chem. Soc.*, 1979, **101**, 4055.

³⁰ G. A. Morris and R. Freeman, *J. Am. Chem. Soc.*, 1979, **101**, 760.

³¹ G. A. Morris, *J. Am. Chem. Soc.*, 1980, **102**, 428.

³² G. Bodenhausen and D. T. Ruben, *Chem. Phys. Lett.*, 1980, **69**, 185.

³³ P. H. Bolton and T. L. James, *J. Am. Chem. Soc.*, 1980, **102**, 1449.

³⁴ G. C. Chingas, R. D. Bertrand, A. N. Garraway, and W. B. Moniz, *J. Am. Chem. Soc.*, 1979, **101**, 4038.

³⁵ G. C. Chingas, A. N. Garraway, R. D. Bertrand, and W. B. Moniz, *J. Magn. Reson.*, 1979, **35**, 283.

³⁶ G. C. Chingas, A. N. Garraway, W. B. Moniz, and R. D. Bertrand, *J. Am. Chem. Soc.*, 1980, **102**, 2520.

Nuclear Overhauser Effect.—In recent years the availability of highly stable superconducting magnets coupled with modern computer control systems has served to extend dramatically the power of traditional assignment techniques in ^1H n.m.r., such as the NOE. This makes such facilities available for the analysis of the ^1H spectra of complex natural products.

Another interesting development is NOE difference spectroscopy (NOEDS). This involves subtracting a control spectrum without NOE from the enhanced spectrum to reveal the changes that occur due to the NOE. In this way it is possible selectively to examine the signals from chosen, small regions of the molecule. A comparable development is decoupling difference spectroscopy (DDS) in which buried multiplets are readily revealed.

NOEDS has been very effectively applied in the assignment of protein^{37,38} and steroid ^1H n.m.r. spectra.³⁹ NOEDS and DDS in conjunction with two-dimensional J spectroscopy, to resolve and analyse the signals, produce a very comprehensive attack on the problem of the complete analysis of the ^1H spectra of complex natural products.

Relaxation by spin diffusion tends to limit the utility of the NOE for studying neighbouring interactions. However, the initial rate of enhancement from the NOE depends accurately upon the inverse sixth power of the internuclear separation and pulse sequences are available for measuring this.⁴⁰ One of them gives a truncated driven NOE (TOE) difference spectrum from which the rate of build up of the FID is derived. Consequently TOEDS provide reliable estimates of interproton distances.

TOEDS and transient NOEDS have been shown to be the most effective, of the currently available techniques, in overcoming spin diffusion in the assignment of individual amide proton signals in the spectrum of basic pancreatic inhibitor.⁴¹ Although the NOE usually arises from the application of a r.f. field of suitable amplitude and frequency the ^1H — $\{^1\text{H}\}$ NOE can also be induced by suitably polarized protons, such as occur in CIDNP experiments. This produces the chemically induced NOE (CINOE), which is advantageous in that the initial polarization can be very large and of either sign; in addition, very broad proton signals can be used.⁴²

3 Solid State N.M.R.

Traditionally, solid state n.m.r. has tended to be the realm of the physicist. Usually solids produce broad n.m.r. signals from which it is not possible to extract very much chemical information. However, single crystal and powder spectra can be employed to determine the shielding tensors for abundant spin- $\frac{1}{2}$ nuclei.^{43–45} In the principal axis system the tensor is diagonalized and the three principal elements are σ_{11} , σ_{22} , and σ_{33} . These elements are normally available from powder spectra as indicated in Figure 5. It is noteworthy that chemical screening anisotropy (CSA) can produce significant signal

³⁷ R. Richarz and K. Wüthrich, *J. Magn. Reson.*, 1978, **30**, 147.

³⁸ K. Wüthrich, G. Wagner, R. Richarz, and S. J. Perkins, *Biochemistry*, 1978, **17**, 2253.

³⁹ L. D. Hall and J. K. M. Sanders, *J. Am. Chem. Soc.*, 1980, **102**, 5703.

⁴⁰ G. Wagner and K. Wüthrich, *J. Magn. Reson.*, 1979, **33**, 675.

⁴¹ A. Dubs, G. Wagner, and K. Wüthrich, *Biochim. Biophys. Acta*, 1979, **577**, 177.

⁴² J. Bargon and G. P. Gardini, *J. Am. Chem. Soc.*, 1979, **101**, 7732.

⁴³ M. Haebleren, *Adv. Magn. Reson., Suppl.*, 1976.

⁴⁴ M. Mehring, 'High Resolution NMR Spectroscopy in Solids', Springer, Berlin, 1976.

⁴⁵ C. P. Slichter, 'Principles of Magnetic Resonance', Springer, Berlin, 1978.

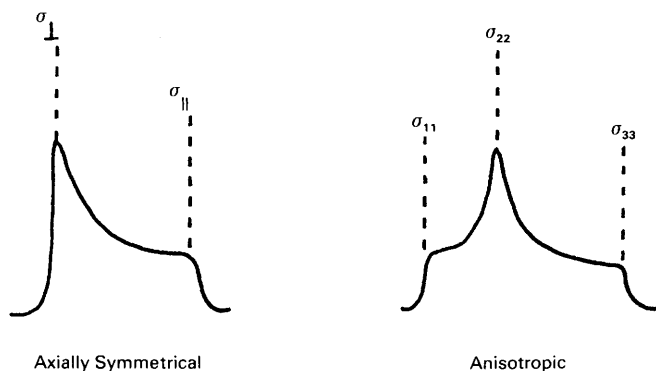


Figure 5 Broadening of n.m.r. signals due to CSA for dipole-decoupled solids that are axially symmetric and fully anisotropic

broadening. However, a more severe source of line broadening in solids is the dipolar spin–spin interaction, which has been removed from the signals presented in Figure 5.

Broad-line N.M.R.—Some proposals of new techniques for investigating broad n.m.r. signals have been presented. Two-dimensional n.m.r. spectroscopy may be applied to unravelling overlapping resonances arising from dipolar couplings.⁴⁶ This technique has been successfully applied to some ^{14}N signals that are broadened due to proton–nitrogen dipolar couplings. The proton decoupled quadrupolar spectrum is presented in one frequency domain while the other contains the dipolar splittings alone. Two-dimensional n.m.r. has also been employed in studies on exchange processes.¹⁷ Included in this work are examples of cross relaxation and spin-diffusion interactions in solids.

Spin-echo methods continue to attract much attention in studies on solids. A technique for the separation of independent echo and transient contributions has been demonstrated for both the general⁴⁷ and hindered rotation cases.⁴⁸ For several examples of deuterium resonances the dipolar interaction dominates the quadrupolar behaviour.^{49,50} By applying a refocusing pulse, or pulse sequence, to the non-observed spins in a heteronuclear dipolar-coupled two-spin system three types of spin echoes may be obtained.⁵¹ In addition to providing information on spin dynamics the echoes yield data on the heteronuclear dipolar interactions. An application of one echo type is in the production of a separated local field two-dimensional spectrum from a single echo train.⁵² For spin- $\frac{1}{2}$ nuclei, coupled to nuclei with large quadrupolar moments, it is possible directly to separate the homonuclear and heteronuclear dipolar contributions to the second moment of their absorption line.⁵³ The homonuclear coupling is obtained

⁴⁶ G. Bodenhausen, R. E. Stark, D. J. Ruben, and R. G. Griffen, *Chem. Phys. Lett.*, 1979, **67**, 424.

⁴⁷ N. Boden and Y. K. Levine, *J. Magn. Reson.*, 1978, **30**, 327.

⁴⁸ I. C. Baionu, N. Boden, Y. K. Levine, and D. Lightowers, *Solid State Commun.*, 1978, **27**, 747.

⁴⁹ N. Boden, S. M. Hanlon, Y. K. Levine, and M. Mortimer, *Chem. Phys. Lett.*, 1978, **57**, 151.

⁵⁰ N. Boden, S. M. Hanlon, Y. K. Levine, and M. Mortimer, *Mol. Phys.*, 1978, **36**, 519.

⁵¹ T. Terao and S. Matsui, *Phys. Rev. B*, 1980, **21**, 3781.

⁵² R. K. Hester, J. L. Ackerman, B. L. Neff, and J. S. Waugh, *Phys. Rev. Lett.*, 1976, **36**, 1081.

⁵³ C. S. Yannoni and R. A. Wind, *J. Magn. Reson.*, 1980, **38**, 493.

from an on-resonance nutation, while the heteronuclear coupling is determined by a line-narrowing experiment.

Techniques for High-resolution Studies.—In order to obtain high-resolution n.m.r. spectra from solids it is necessary not only to remove the dipolar and CSA broadenings but in the case of rare nuclei, such as ^{13}C or ^{15}N , long relaxation times have to be dealt with. It is the application of experimental techniques that can cope with these problems that has made solid state n.m.r. such an exciting prospect for chemists.^{54,55}

For rare nuclei the dipolar broadening arises largely from interactions with abundant nuclei. These interactions may be decoupled by high power double resonance techniques.⁵⁶ Multiple pulse sequences are often employed in this context.⁵⁷ Magic angle sample spinning (MASS) is usually performed to remove line broadenings due to CSA and any dipolar interactions between the rare spins themselves.⁵⁸ Cross polarization (CP) circumvents the long relaxation time problem. There are a number of ways of performing the experiment; usually, multiple Hartmann–Hahn contacts are sought. In this way the abundant spin polarization is lost by CP and by spin–lattice relaxation in the rotating frame. Thus the value of $T_{1\rho}$ for these spins may be obtained.

For abundant nuclei the experimental problems differ from those of rare nuclei. A limitation to high-resolution proton n.m.r. studies on solids has been that the available WAHUA 4-pulse and MREV 8-pulse cycles are only suitable for samples with weak homonuclear dipolar coupling. This situation has been substantially rectified by the introduction of 24-pulse and 52-pulse cycles.⁵⁹

The 24-pulse cycle has been used to determine the proton shielding tensor for the water molecule in α -oxalic acid dihydrate, which is not available from measurements with the 8-pulse cycle.⁶⁰ Examples of the high resolving power produced by the 52-pulse cycle are furnished by single crystal studies of gypsum⁶¹ and hexagonal ice.⁶²

Double quantum n.m.r. is a useful way to obtain the spectra of quadrupolar nuclei in solids. Three versions of double resonance detection of double quantum spectra have been described.⁶³ They are, direct detection of the CP double quantum decay, indirect detection of the frequency spectrum, and indirect detection of the FID.

The ‘forbidden’ deuterium double quantum transitions are independent, to first order, of the quadrupole coupling. Consequently the double quantum spectra of polycrystalline and amorphous solids usually consist of overlapping CSA powder patterns.⁶⁴ The CSA is removed by MASS to afford double quantum lines, which are significantly less sensitive to spinner angle adjustment than are the single quantum

⁵⁴ J. Schaefer and E. O. Stejskal, in ‘Topics in ^{13}C NMR Spectroscopy’, ed. G. C. Levy, Wiley, New York, 1979, Vol. 3, p. 283.

⁵⁵ D. A. Torchia and D. L. Vanderhart, in ‘Topics in ^{13}C NMR Spectroscopy’, ed. G. C. Levy, Wiley, New York, 1979, Vol. 3, p. 325.

⁵⁶ A. Pines, M. G. Gibby, and J. S. Waugh, *J. Chem. Phys.*, 1973, **59**, 569.

⁵⁷ A. N. Garroway, *J. Magn. Reson.*, 1977, **28**, 365.

⁵⁸ E. R. Andrew, in ‘Progress in NMR Spectroscopy’, ed. J. Emsley, J. Feeney, and L. H. Sutcliffe, Pergamon, London, 1972, Vol. 8, p. 1.

⁵⁹ D. P. Burum and W. K. Rhim, *J. Chem. Phys.*, 1979, **71**, 944.

⁶⁰ B. Berglund and R. W. Vaughan, *J. Chem. Phys.*, 1980, **72**, 3424.

⁶¹ D. P. Burum and W. K. Rhim, *J. Magn. Reson.*, 1979, **34**, 241.

⁶² W. K. Rhim, D. P. Burum, and D. D. Elleman, *J. Chem. Phys.*, 1979, **71**, 3139.

⁶³ S. Vega, T. W. Shattuck, and A. Pines, *Phys. Rev. A*, 1980, **22**, 638.

⁶⁴ A. Pines, S. Vega, and M. Mehring, *Phys. Rev. B*, 1978, **18**, 112.

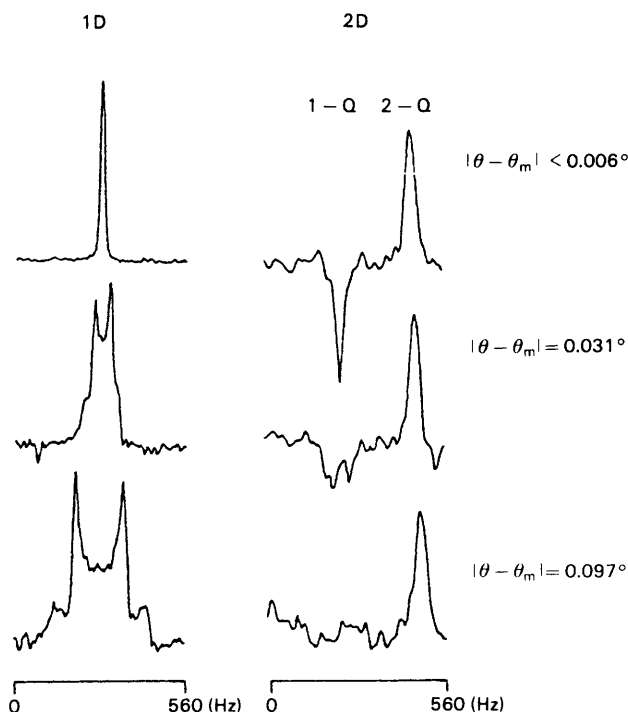


Figure 6 One-dimensional (1D) and two-dimensional (2D) deuterium solid state spectra of polycrystalline 28% randomly deuterated ferrocene- d_{10} rotating at 1.11 kHz (Reproduced by permission from *Chem. Phys. Lett.*, 1980, **74**, 377)

resonances.⁶⁵ This is demonstrated in Figure 6 for the one- and two-dimensional deuterium spectra of polycrystalline 28% randomly deuterated ferrocene- d_{10} rotating at 1.11 kHz, where $|\theta - \theta_m|$ represents the deviation from the magic angle. The one-dimensional spectra show line narrowing of the powder pattern as θ approaches the magic angle, θ_m . In the two-dimensional spectra the single quantum ($1 - Q$) and double quantum ($2 - Q$) lines are presented.

As θ deviates from θ_m the single quantum line splits into the quadrupole powder pattern and is lost in the noise while the double quantum line remains sharp. Hence it seems likely that double quantum n.m.r. with MASS will provide high-resolution deuterium spectra, without very stringent spinner requirements, for complicated molecules containing a number of inequivalent deuterium sites. Another aspect of MASS that has to be considered is that it can produce level crossing, which may partially restore deuteron spin diffusion otherwise quenched by the orientational dependence of the quadrupole splitting.⁶⁶

Some Applications of High-resolution Studies.—The range of applications for high-resolution n.m.r. techniques is very large and extends to all forms of solids,

⁶⁵ R. Eckman, L. Müller, and A. Pines, *Chem. Phys. Lett.*, 1980, **74**, 376.

⁶⁶ M. Alla, R. Eckman, and A. Pines, *Chem. Phys. Lett.*, 1980, **71**, 148.

including fibres, gels, membranes, glasses, rubbers, and adsorbed species. Discussions of some of these are to be found elsewhere.^{1,54,55} Only a very few recent examples are presented here in the hope of giving a glimpse of the type of results that are now routinely available.

CP/MASS is the most commonly employed procedure for 'rare' nuclei. An example is given in Figure 7 of a ²⁹Si solid state spectrum, which shows clearly the two types of

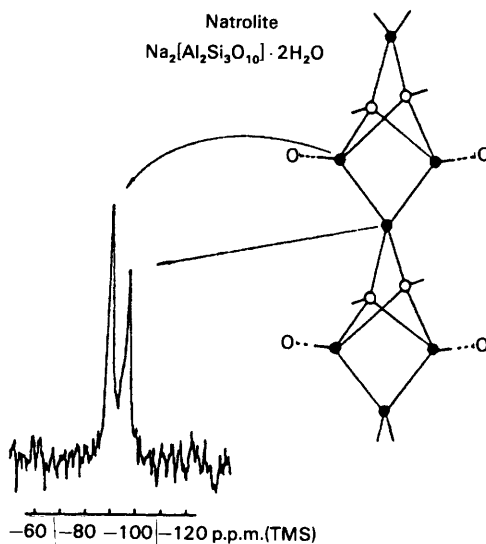


Figure 7 Solid state ²⁹Si n.m.r. spectrum and schematic structure of natrolite (●, silicon; ○, aluminium: only the central atoms of the tetrahedra are shown) (Reproduced by permission from *J. Am. Chem. Soc.*, 1980, **102**, 4892)

silicon present in natrolite.⁶⁷ One type is connected to three aluminium oxygen tetrahedra and the other is connected to only two. They appear in the ratio of 2 : 1 as is shown by the intensities of the two lines in Figure 7.

The most commonly studied of the 'rare' nuclei is ¹³C. Figure 8 shows the ¹³C CP/MASS spectrum of a microcrystalline sample of cellulose,⁶⁸ together with the peak assignments. The overlap of the signals from carbons 2, 3, and 5 arises from their chemical similarity. From relaxation measurements it is concluded that the splitting of the carbon-4 resonance and the shoulder on the carbon-6 signal imply that the glucose units are found in two magnetically inequivalent environments in dry cellulose 1. It is apparent that cellulose is a complex system and that further data are required for a complete analysis.^{68,69}

Since the ¹³C high-resolution spectra of solids are comparable to those for solutions

⁶⁷ E. Lippmaa, M. Mägi, A. Samoson, G. Engelhardt, and A. R. Grimmer, *J. Am. Chem. Soc.*, 1980, **102**, 4889.

⁶⁸ W. L. Earl and D. C. Vanderhart, *J. Am. Chem. Soc.*, 1980, **102**, 3251.

⁶⁹ R. H. Atalla, J. C. Gast, D. W. Sindorf, V. J. Bartuska, and G. E. Maciel, *J. Am. Chem. Soc.*, 1980, **102**, 3249.

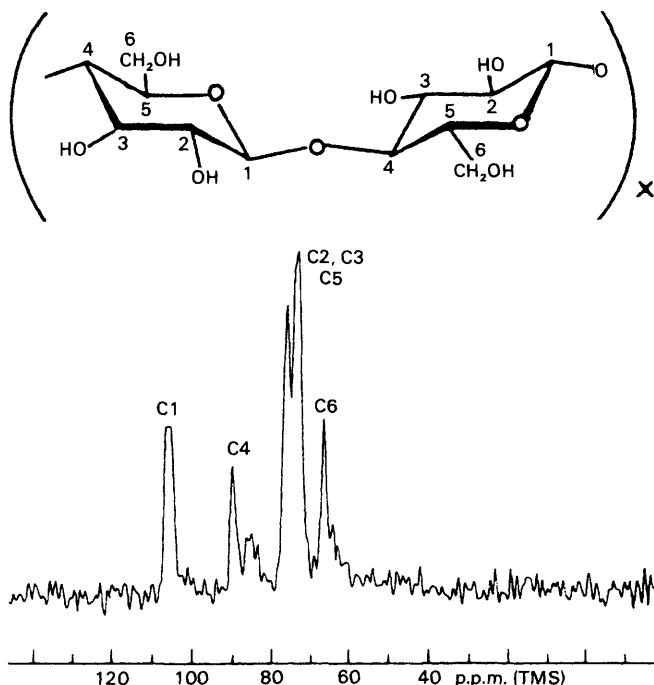


Figure 8 The CP/MAS ^{13}C spectrum of a dried sample of microcrystalline cellulose 1 (Reproduced by permission from *J. Am. Chem. Soc.*, 1980, **102**, 3251)

it is a simple process to identify features peculiar to the solid state. Both glucose and cellulose exhibit different ^{13}C shieldings for their solid, in comparison with their solution, spectra. These differences may be attributed to solid state packing effects or, more probably, hydrogen bonding in the solid.⁶⁸ Irrespective of their origin such solid state effects can lead to problems of signal assignment.

In contrast, assignment is facilitated for ^{13}C nuclei bonded to nitrogen by means of a solid state effect that causes line broadening and splitting to occur.⁷⁰ A particular example is furnished by $\geq\text{CNH}_3^+$ groups in some amino-acid zwitterions; the ^{13}C signal is split into a doublet with a separation of about 100 Hz. Figure 9 shows this effect in the ^{13}C spectra of the zwitterionic forms of (A) glycine, (B) L-alanine, and (C) L-valine. It seems likely that the splitting arises from the opposing quantization effects on the ^{14}N nucleus due to the internal electric-field gradient on the one hand and the applied magnetic field on the other. Consequently the splitting should be reduced at higher fields and/or when the electric field gradient is decreased. Support for this proposal is provided by the observation of a single line for the methylene carbons in the spectrum of tetraethylammonium bromide.⁷⁰

A further point of interest in Figure 9 (C) is that the methyl signals of the isopropyl group are separated by 2.6 p.p.m. The corresponding value in solution is 1.2 p.p.m.

⁷⁰ C. J. Groombridge, R. K. Harris, K. J. Packer, B. J. Say, and S. F. Turner, *J. Chem. Soc., Chem. Commun.*, 1980, 174.

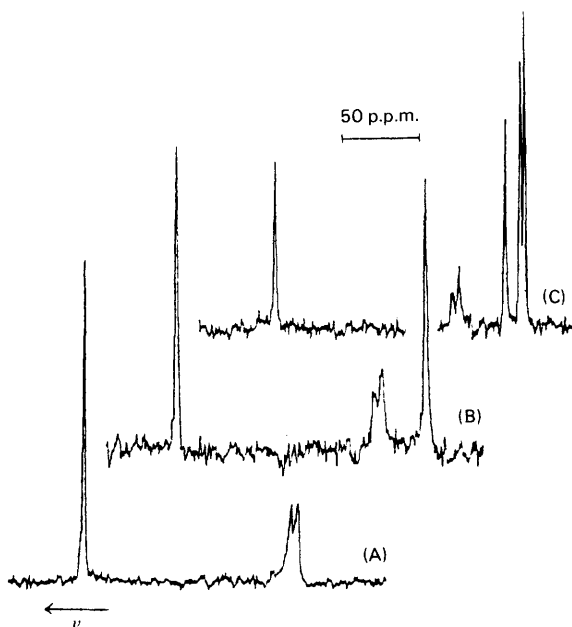


Figure 9 22.6 MHz ^{13}C n.m.r. spectra of some solid amino-acids; (A) glycine; (B) L-alanine; (C) L-valine
(Reproduced by permission from *J. Chem. Soc., Chem. Commun.*, 1980, 175)

The solution splitting is attributed to the chirality of the sample, the additional splitting in the solid state spectrum probably being due to restricted C—C single bond rotation.

Solid state high-resolution n.m.r. spectra for abundant nuclei may be obtained simply by means of the MASS technique alone. Examples are to be found amongst those polymers and related materials that undergo rapid but restricted motion and thus give 'super-Lorentzian' proton spectra. Some inorganic compounds with nuclei having short T_1 values are also suitable for studies using only MASS. An example is provided by polycrystalline phosphorus pentachloride. The ^{31}P n.m.r. spectrum of the static sample has two signals, 540 and 695 Hz in width, which are attributed to PCl_4^+ and PCl_6^- , respectively.⁷¹ The application of MASS reduces the line widths of both signals to about 30 Hz.

4 Nuclear Relaxation Processes

In recent years the number of publications relating to spin relaxation processes in pure liquids and simple solutions has decreased, while those dealing with gases has never been very large.

However, developments in computer and n.m.r. software and hardware have lead to an increasing interest in spin relaxation in more complicated systems, such as polymers and paramagnetic solutions.

⁷¹ D. J. Burton, R. K. Harris, and L. H. Merwin, *J. Magn. Reson.*, 1980, **39**, 159.

Pure Liquids.—Most work in this area has been concerned with the dynamic behaviour of molecules in the liquid state, interest in which has increased considerably in recent years.⁷² From intramolecular relaxation processes it is possible to determine the reorientational correlation time or the angular velocity correlation time. However, the evaluation of time correlation functions is a difficult problem. Consequently much work is directed to the study of small model compounds.⁷³

Recent experimental developments include the measurement of correlation times as a function of density and temperature and the determination of self diffusion coefficients by spin-echo techniques. Work of this kind has been performed on carbon monoxide by means of ¹³C studies.⁷⁴ Values for T_1 , T_2 , and the self-diffusion coefficient are reported at temperatures between freezing point and 110 K at pressures up to 173 MPa. Analysis reveals that the spin-rotation interaction is the dominant relaxation process. By combining the carbon monoxide results with those available from liquid nitrogen, it appears that both molecules have the same angular velocity correlation times over the temperature range considered.

Some investigations have been concerned with spin relaxation in water under extreme conditions, as exemplified by the measurement of deuterium relaxation times in heavy water at temperatures down to 188 K and at pressures up to 300 MPa.⁷⁵ The increase in T_1 with pressure, in the isotherms above 240 K, is more pronounced than it is in the proton case. By assuming isotropic reorientation the deuteron nuclear quadrupole coupling constant is evaluated and found to be in good agreement with estimates from other sources.

The increased accuracy of spin-echo experiments⁷⁶ permits the measurement of self-diffusion coefficients with a precision of about $\pm 1\%$. Use has been made of this accuracy in a study of the ¹⁶O—¹⁸O isotope effect on the translational motion of water molecules in the temperature range of 277–333 K and at pressures up to 300 MPa. The ratio of the H₂¹⁶O and H₂¹⁸O self-diffusion coefficients is constant over the region studied as predicted by classical theories.

Non-electrolyte Solutions.—Spin-relaxation studies on non-electrolyte solutions usually fall into one of three categories. The first is aimed at the determination of the dynamic behaviour of a molecule considered to be dissolved in an inert medium. ¹³C relaxation data are commonly employed in this instance so that the molecular motions can be probed at various skeletal sites.

The second type of investigation deals with molecular association in liquid mixtures. This area has become quite active in recent years. Finally, spin-relaxation studies have been used to throw light on the nature of the various mechanisms contributing to a given relaxation behaviour.

Studies on anisotropic and internal molecular motions are usually based on the fundamental theoretical work of Woessner.⁷⁷ An example of work of this kind relates to the ¹³C relaxation of the various carbon sites of benzofuran and thirteen of its

⁷² W. A. Steele, in 'Advances in Chemical Physics', ed. I. Prigogine and S. A. Rice, Wiley, New York, 1976, Vol. 34, p. 1.

⁷³ R. E. D. McClung, *Adv. Mol. Relaxation Processes*, 1977, **10**, 83.

⁷⁴ E. Fukushima, A. A. V. Gibson, and T. A. Scott, *J. Chem. Phys.*, 1979, **71**, 1531.

⁷⁵ E. Lang and H. D. Lüdemann, *Ber. Bunsenges. Phys. Chem.*, 1980, **84**, 462.

⁷⁶ K. R. Harris, R. Mills, P. J. Black, and D. S. Webster, *J. Magn. Reson.*, 1978, **29**, 473.

⁷⁷ D. E. Woessner, *J. Chem. Phys.*, 1962, **37**, 647.

methyl-substituted derivatives.⁷⁸ NOE data assist in the separation of the dipole–dipole and spin–rotation contributions of the relaxation. The anisotropy of the benzofuran motion depends upon the number and positions of the methyl groups, while the internal rotation of these groups appears to be very position dependent. It is noteworthy that some doubts have been raised about the validity of results obtained by an uncritical application of Woessner's equation;^{79,80} perhaps the time is ripe for some theoretical developments in this field.

An illustration of work on molecular association in liquid mixtures is provided by the study of hydrogen bonding between pyridine and 2-dichlorophenol-OD.⁸¹ The formation of the hydrogen bond retards the motion of both molecules about axes perpendicular to the hydrogen-bond axis, whereas motions parallel to this axis appear to be almost uninfluenced. Most studies on the elucidation of the contributions of various processes to the spin relaxation mechanism relate to spin- $\frac{1}{2}$ nuclei other than protons. Work on ⁷⁷Se is mentioned as being typical of this area.^{82,83} Methyl spin-rotation interactions dominate the ⁷⁷Se relaxation of methyl hydrogen selenide dissolved in deuteriochloroform. However, for a variety of dialkyl selenides, dialkyl and diaryl diselenides, selenols, and selenonium compounds, the ⁷⁷Se relaxation appears to be controlled by the spin rotation and CSA interactions. An exception is made in the case of some of the larger molecules for which the dipole–dipole interaction appears to replace the spin–rotation interaction as a significant relaxation contributor.

Electrolyte Solutions.—There is current interest in the relaxation processes occurring in both diamagnetic and paramagnetic electrolyte solutions.¹ In diamagnetic systems the relaxation of most solvent and ionic species is fairly well understood. This is especially true for 1:1 electrolytes, and thus attention is now being turned onto solutions containing di- and tri-valent ions. Recent instrumental developments allow the alkaline-earth nuclei, with their low n.m.r. sensitivity and natural abundance, to be measured at low salt concentrations. Thus relaxation processes for these conditions can be studied. As an example of a diamagnetic electrolyte study, ¹³⁵Ba and ¹³⁷Ba relaxation in aqueous solutions of barium chloride, bromide, and iodide concentrations as low as 0.1 m have been reported.⁸⁴ The quadrupolar relaxation process is the dominant one.

Much current interest is concentrated in spin-relaxation studies of paramagnetic systems. The details of the relaxation process are considerably more complex than for diamagnetic systems. Even in the simple Ni²⁺–water system it seems that the Solomon–Bloembergen–Morgan theory is inadequate as a means of understanding the relaxation process.^{85,86} Water exchange in solutions containing Ni²⁺ and Mn²⁺ has been studied as a function of temperature and pressure^{87,88} by means of ¹⁷O relaxation

⁷⁸ N. Platzer, *Org. Magn. Reson.*, 1978, **11**, 350.

⁷⁹ P. Stilbs and M. E. Moseley, *J. Magn. Reson.*, 1979, **33**, 209.

⁸⁰ B. Blicharska, H. G. Hertz, and H. Versmold, *J. Magn. Reson.*, 1979, **33**, 531.

⁸¹ A. Kratochwill, R. L. Vold, and R. R. Vold, *J. Chem. Phys.*, 1979, **71**, 1319.

⁸² J. D. Odom, W. H. Dawson, and P. D. Ellis, *J. Am. Chem. Soc.*, 1979, **101**, 5815.

⁸³ H. Jakobsen, A. J. Zozulin, P. D. Ellis, and J. D. Odom, *J. Magn. Reson.*, 1980, **38**, 219.

⁸⁴ O. Lutz and H. Oehler, *Z. Phys. A*, 1978, **288**, 11.

⁸⁵ H. L. Friedman, M. Holz, and H. G. Herz, *J. Chem. Phys.*, 1979, **70**, 3369.

⁸⁶ J. J. Led, *Mol. Phys.*, 1980, **40**, 1293.

⁸⁷ Y. Ducommun, W. L. Earl, and A. E. Merbach, *Inorg. Chem.*, 1979, **18**, 2754.

⁸⁸ Y. Ducommun, K. E. Newman, and A. E. Merbach, *Helv. Chim. Acta*, 1979, **62**, 2511.

of the free water molecules. The activation parameters obtained support a dissociative interchange mechanism for the solutions containing Ni^{2+} , whereas an associative interchange model is favoured in the presence of Mn^{2+} .

Polymer Solutions.—In the case of polymer solutions the major relaxation interest appears to reside in the relationship between the measured relaxation data and polymer segmental motions. Several authors have proposed motional models from which expected relaxation times may be calculated.¹ Backbone segmental motions have been treated by a sharp cut off model⁸⁹ and by a diamond lattice motional model.⁹⁰ The former of these has been successfully applied to poly(2,6-dimethyl-1,4-phenylene oxide),^{91,92} which in addition to the segmental motions, exhibits rotation of the rings about the *para* backbone bonds and internal rotation of the methyl side groups.

The diamond lattice model has been employed in studies on polystyrene⁹³ and on predominantly syndiotactic poly(methylmethacrylate) in a range of solvents.⁹⁴ In the second of these reports it is concluded that the rate of backbone motion depends on the solvent viscosity in good solvents, whereas in poor solvents the backbone motion is more hindered than can be anticipated on the basis of solvent viscosity alone. The rate of α -methyl rotation appears to be independent of the chosen solvent.

Both the diamond lattice conformational jump model and the sharp cut off model consider discrete conformational transitions. A continuum description of these discrete models has been presented,⁹⁵ which imposes short and long wavelength cut offs in the frequency spectrum. The short wavelength cut off corresponds to the dimensions of the smallest displaceable unit, while the long wavelength cut off relates to the length of polymer chain over which motional correlation is lost. When applied to the ^1H and ^{13}C relaxation data of some bulk rubbers and polymers in solution intuitively reasonable results are obtained.

Multiple internal rotations of polymer side chains have been treated by a model dealing with random jumps among three sites⁹⁶ and by restricted diffusion and jump models.⁹⁷ Satisfactory applications of these models to measured relaxation data are provided.

The dynamics of entangled polymer chains in concentrated solutions, with residual dipolar coupling, have been considered.⁹⁸ It is shown that the assumption of the critical motion being that of the slowest Rouse mode of the chain leads to a prediction of the chain length. In addition the temperature dependence of the concentration at which polymer coil overlap occurs leads to a non-zero average dipolar coupling being present.

A different approach to the relationship between relaxation data and polymer motion is by means of a general formalism based on the theory of Markov processes.⁹⁹

⁸⁹ A. A. Jones and W. H. Stockmayer, *J. Polym. Sci., Polym. Phys. Ed.*, 1977, **15**, 847.

⁹⁰ B. Valeur, J. P. Jarry, F. Geny, and L. Monverie, *J. Polym. Sci., Polym. Phys. Ed.*, 1975, **13**, 667.

⁹¹ A. A. Jones, G. L. Robinson, F. E. Gerr, M. Biscaglia, S. L. Shostak, and R. P. Lubianez, *Macromolecules*, 1980, **13**, 95.

⁹² R. P. Lubianez and A. A. Jones, *J. Magn. Reson.*, 1980, **38**, 331.

⁹³ F. Heatley and B. Wood, *Polymer*, 1979, **20**, 1512.

⁹⁴ F. Heatley and M. K. Cox, *Polymer*, 1980, **21**, 381.

⁹⁵ J. T. Bendler and R. Yaris, *Macromolecules*, 1978, **11**, 650.

⁹⁶ A. Tsutsumi and C. Chachaty, *Macromolecules*, 1979, **12**, 429.

⁹⁷ R. J. Wittebort and A. Szabo, *J. Chem. Phys.*, 1978, **69**, 1722.

⁹⁸ J. P. Cohen-Addad, *J. Chem. Phys.*, 1979, **71**, 3689.

⁹⁹ R. King and O. Jardetzky, *Chem. Phys. Lett.*, 1978, **55**, 15.

This allows the analysis of spin relaxation in systems with multiple degrees of freedom. Consequently, a systematic testing and comparison of various models is permitted that contrasts with the simple calculation of correlation times from molecular motion models chosen on an *ad hoc* basis. By means of this general formalism it is possible to map the internal motions of proteins. An application is presented in terms of the analysis of ^{13}C relaxation in the bovine pancreatic trypsin inhibitor.¹⁰⁰ Emphasis is laid on the importance of comparing T_1 , T_2 , and NOE data obtained at two or more applied field strengths. In this approach there is no *a priori* choice of molecular motion. Instead the experimental data are analysed to provide a range of allowed motional frequencies and their relative contributions to the relaxation are calculated for each group in the polymer.

The results obtained for the bovine pancreatic trypsin inhibitor reveal that, in addition to side-chain rotation and diffusional tumbling, there are both a very rapid ($\sim 10^{11} \text{ s}^{-1}$) and a relatively slow ($\sim 10^8 \text{ s}^{-1}$) component in the motion of the backbone. It is alleged that neither of these motions is detected when inadequate data and limited models are employed.¹⁰⁰

Gases.—In principle, gas-phase experiments are more suitable for theoretical interpretation than are those on condensed phases and thus are, in general, better understood. Experimental improvements permit the measurement of relaxation data to be extended to relatively low-pressures. In this region new theoretical problems present themselves. In particular the behaviour of T_2 at low densities is the subject of some controversy.^{101,102}

At low densities the correlation time becomes so long that it approaches the microscopic time scale, thus rendering the Markovian approximation invalid. The Bloch equations also break down under these conditions as is best witnessed by a consideration of the relaxation of the magnetization in the frequency domain.¹⁰³

5 Theoretical Aspects of N.M.R. Parameters

Advances in theoretical understanding of nuclear shielding, spin–spin coupling, and spin relaxation are largely concentrated on nuclei from the first two rows of the periodic table. There appears to be two main reasons for this. First, it is generally anticipated that the n.m.r. parameters of the heavier nuclei will be determined by the same factors as those responsible for the lighter nuclei. Secondly, MO computations are more readily, and more cheaply, performed on molecules containing the lighter nuclei.

Nuclear Shielding.—The gauge problems associated with the formulation of the screening tensor by Ramsey's method are usually overcome by means of MO techniques employing linear combinations of gauge dependent atomic orbitals. The calculation can then be performed at either the *ab initio* or semi-empirical level.¹⁰⁴ A

¹⁰⁰ A. A. Ribeiro, R. King, C. Restivo, and O. Jardetzky, *J. Am. Chem. Soc.*, 1980, **102**, 4040.

¹⁰¹ F. R. McCourt and G. Terti, *Chem. Phys.*, 1978, **32**, 23.

¹⁰² B. C. Sanctuary and R. F. Snyder, *J. Chem. Phys.*, 1977, **67**, 4511.

¹⁰³ B. C. Sanctuary and L. Selwyn, *J. Chem. Phys.*, 1978, **69**, 2157.

¹⁰⁴ K. A. K. Ebraheem and G. A. Webb, in 'Progress in NMR Spectroscopy', ed. J. Emsley, J. Feeney, and L. H. Sutcliffe, Pergamon, London, 1977, Vol. 11, p. 149.

number of *ab initio* calculations on nuclei from the first two rows of the periodic table have been reported.¹ However, the computing problems and expenditure involved have so far prevented the heavier nuclei from being so treated. To some extent these difficulties can be alleviated by substituting a pseudopotential for the inner electronic shells and using only the valence shells for calculations of the shielding tensor. Results obtained by this procedure have been reported for the ²⁹Si, ³¹P, ³³S, and ³⁵Cl nuclei in SiH₄, PH₃, H₂S, and HCl.¹⁰⁵ Although the basis sets used are not optimized the results are encouraging. The errors found in the paramagnetic component of the shielding tensor are drastically reduced by improving the basis set used.

Comparison of the pseudopotential results for ³¹P in PH₃ with those obtained from all electron calculations^{106,107} and experiment shows that the pseudopotential approach overestimates the average value of the screening tensor by about 55 p.p.m. In comparison with this the all electron *ab initio* calculations produce a corresponding result which lies within 20 p.p.m. of that measured. ³¹P nuclear shielding is widely used in studies on the backbones of nucleic acids and on the polar head groups of phospholipids. Consequently, calculations of ³¹P shielding in model compounds of biological phosphates are important.¹⁰⁸ From calculations on the anions X₂PO₄⁻, where X is Me or H, it appears that the ³¹P shielding is mainly determined by the geometry of the various conformers. It is predicted¹⁰⁸ that the ³¹P shielding difference between the *gauche-gauche* and *gauche-trans* conformers is in the range of 3.5 to 6.5 p.p.m., with the latter conformer presenting the more highly shielded phosphorus environment.

Molecular electronic properties such as nuclear shielding and spin-spin coupling are commonly evaluated at the semi-empirical level by incorporating a perturbation technique. The most frequently employed procedures are the sum-over-states (SOS) and finite perturbation theory (FPT) methods. Some SOS calculations of the shielding of first-row nuclei illustrate the advantages of using the CNDO/S and INDO/S parameterizations rather than the MINDO/3 parameters for calculations of second-order molecular properties such as nuclear shielding.¹⁰⁹⁻¹¹³ This appears to result from the fact that the CNDO/S and INDO/S parameter sets are based upon electronic excitation processes whereas the MINDO/3 parameters are derived from molecular ground state properties.

A modification of the CNDO/S parameterization has considered the orbital exponents to be dependent upon the electronegativity difference between directly bonded atoms.¹¹⁴ This appears to give reasonable results for some ¹³C and ³¹P shieldings and their anisotropies.

The FPT approach to ¹³C shielding calculations has been reformulated to incorporate a new set of parameters chosen by a least-squares procedure so as to fit

¹⁰⁵ J. Ridard, B. Levy, and P. Millie, *Mol. Phys.*, 1978, **36**, 1025.

¹⁰⁶ P. Lazzeretti and R. Zanasi, *J. Chem. Phys.*, 1980, **72**, 6768.

¹⁰⁷ F. Keil and R. Ahlrichs, *J. Chem. Phys.*, 1979, **71**, 2671.

¹⁰⁸ F. R. Prado, C. Giessner-Pretre, B. Pullman, and J. P. Daudey, *J. Am. Chem. Soc.*, 1979, **101**, 1737.

¹⁰⁹ M. Jallali-Heravi and G. A. Webb, *Org. Magn. Reson.*, 1978, **11**, 524.

¹¹⁰ M. Jallali-Heravi and G. A. Webb, *J. Magn. Reson.*, 1978, **32**, 429.

¹¹¹ M. Jallali-Heravi and G. A. Webb, *J. Mol. Struct.*, 1979, **55**, 113.

¹¹² M. Jallali-Heravi and G. A. Webb, *Org. Magn. Reson.*, 1979, **12**, 174.

¹¹³ C. Collier and G. A. Webb, *Org. Magn. Reson.*, 1979, **12**, 659.

¹¹⁴ P. Bernard-Moulin and G. Pouzard, *J. Chim. Phys. Phys. Chim. Biol.*, 1979, **76**, 708.

some experimental data for model compounds.¹¹⁵ The requirement of new parameter sets for each set of molecules considered by the FPT procedure tends to imply that the predictive capacity of this method is not too high. In contrast, the SOS calculations of nuclear shielding are reasonably successful at predicting chemical shift variations by means of parameter sets, such as CNDO/S and INDO/S, which are taken from work relating to other molecular properties.

Interest in the current-density approach to nuclear shielding has recently been revived.^{116,117} The current density can be obtained from the classical equations of motion of the electron density¹¹⁸ and expressed in terms of paramagnetic and diamagnetic current-density components. For the hydrogen molecule good agreement with a previous result for the shielding tensor¹¹⁶ is reported.

The shielding-density function is a surface in four-dimensional space. Plots of charge density on a particular plane in molecule-fixed axes may be represented by maps of surfaces. Such maps are useful in discussions of bonding and force constants. Similarly, shielding density maps can be employed in chemical shift interpretations as illustrated for hydrogen fluoride.¹¹⁷ This molecule has also been considered in some *ab initio* calculations of the electric-field dependence of nuclear shielding.¹¹⁹

Despite some controversy the concept of 'ring currents' has been widely used in the interpretation of proton chemical shifts of benzenes, poly condensed hydrocarbons, and of large monocyclic polyenes. The relationship of 'ring current' to another non-observable, 'aromaticity', has been considered in a recent review.¹²⁰ Since the idea of a 'ring current' contribution to nuclear shielding implies a partitioning of the shielding tensor in some undefined way, it follows that approximate calculations are necessarily involved.

All electron coupled Hartree-Fock calculations are unsuitable for this purpose because the one- and two-electron integrals concerned involve all of the orbitals. One assumption usually made is that of σ - π separability. A model has been proposed¹²¹ in which the π electrons are localized and the σ electrons are considered to make local and non-local contributions to the proton shielding. The results for 65 proton environments in condensed hydrocarbons show deviations of less than 0.2 p.p.m. for 82% of the cases considered. From these calculations it appears that it is not necessary to associate a special 'ring current' effect with π electrons. Another approach is to divide the nuclear shielding into a number of contributions amongst which is one due to local anisotropies. This procedure has been applied to a number of cyclic polyenes, which contain both inner and outer proton sites.^{122,123} The results show that the local anisotropy contributions are larger for the inner than for the outer sites.

One difficulty in comparing theoretical and experimental determinations of nuclear shielding is that the latter may include contributions induced by the local fields generated by the molecular environment. This applies to measurements on solids and

¹¹⁵ A. R. Garger, P. D. Ellis, K. Seidman, and K. Schade, *J. Magn. Reson.*, 1979, **34**, 1

¹¹⁶ K. Salzer, *Ann. Phys. (Leipzig)*, 1979, **36**, 91.

¹¹⁷ C. J. Jameson and A. D. Buckingham, *J. Phys. Chem.*, 1979, **83**, 3366.

¹¹⁸ K. Salzer and H. Schmiedel, *Ann. Phys. (Leipzig)*, 1977, **34**, 415.

¹¹⁹ M. Zaucer and A. Azman, *Z. Naturforsch., Teil A*, 1979, **34**, 1279.

¹²⁰ R. B. Mallion, *Pure Appl. Chem.*, 1980, **52**, 1541.

¹²¹ P. H. Blustin, *Mol. Phys.*, 1980, **39**, 565.

¹²² H. Vogler, *J. Mol. Struct.*, 1979, **51**, 289.

¹²³ H. Vogler, *Tetrahedron Lett.*, 1979, 229.

matrix isolated species as well as to those on partially oriented molecules in a liquid crystal. The latter of these also suffer from the difficulties associated with determining the order parameter.

The shielding anisotropy induced in a caesium ion by a lyophilic mesophase is found to be dependent on the relative orientations of the magnetic field and the mesophase director. The maximum induced anisotropy is 3 p.p.m.¹²⁴ A similar investigation on the fluoride ion in lyotropic liquid crystals reveals that the induced anisotropy depends upon the composition of the chosen sample.¹²⁵ With respect to zero for the anisotropy of the free ion the measured data range from -19.4 to $+6.6$ p.p.m.

These induced anisotropies imply that results obtained in liquid-crystal media are probably unsuitable for comparison with theoretical estimates of shielding anisotropies for isolated molecules.

The effect of intermolecular interactions on nuclear shielding have been studied by means of *ab initio* calculations on the H_2 -He interacting pair¹²⁶ and on the lithium ion in the presence of water, ammonia, or methanol.¹²⁷ The first of these two systems relates to the effects of van der Waals' forces and the second to the formation of strong molecular complexes. The results are encouraging and in the case of the studies on lithium ions, the experimental chemical shifts are correctly reproduced only when four molecules in the first solvation shell are included in the calculation.

Solvation effects on the shielding of some first-row nuclei have been estimated by means of the solvation model. Both SOS calculations with INDO/S parameters and FPT calculations with INDO parameters have been employed.¹²⁸⁻¹³⁰ Comparison with the available experimental data suggests that both sets of calculations provide reasonable results. In those cases where there is a divergence between the predictions obtained by the two calculational procedures it seems that the SOS method is to be preferred.

Nuclear shielding is one of the molecular electronic properties which depends upon the rotational and vibrational states of a molecule. In n.m.r. the timescale is such that an average overall rovibrational state is observed. Thus for an isolated molecule the shielding is temperature dependent owing to a variation of the populations of the rovibrational states.¹³¹

The effects of vibrations and rotations on the shielding of ^{11}B , ^{13}C , ^{15}N , ^{19}F , and ^{31}P nuclei in a variety of molecules have been presented.¹³² The temperature-dependent shieldings are observed in the gas phase at the zero-pressure limit in order to eliminate intermolecular interactions. The largest shielding effects are found in the ^{19}F data.

Spin-Spin Coupling.—Calculations of nuclear spin-spin couplings are usually based on a MO approach to the contact (C), orbital (O), and dipolar (D) expressions

¹²⁴ F. Y. Fujiwara and L. W. Reeves, *Mol. Phys.*, 1978, **36**, 1897.

¹²⁵ O. Söderman, A. Khan, and G. Lindblom, *J. Magn. Reson.*, 1979, **36**, 141.

¹²⁶ J. P. Riley, I. H. Hillier, and W. T. Raynes, *Mol. Phys.*, 1979, **38**, 353.

¹²⁷ F. R. Prado, C. Giessner-Prettre, J. P. Daudey, A. Pullman, J. F. Hinton, G. Young, and D. Harpool, *J. Magn. Reson.*, 1980, **37**, 431.

¹²⁸ I. Ando, M. Jallali-Heravi, M. Kondo, S. Watanabe, and G. A. Webb, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 2240.

¹²⁹ M. Jallali-Heravi and G. A. Webb, *Org. Magn. Reson.*, 1980, **13**, 116.

¹³⁰ I. Ando, M. Jallali-Heravi, M. Kondo, B. Na Lamphun, S. Watanabe, and G. A. Webb, *Org. Magn. Reson.*, 1980, **14**, 92.

¹³¹ G. Riley, W. T. Raynes, and P. W. Fowler, *Mol. Phys.*, 1979, **38**, 877.

¹³² C. J. Jameson, A. K. Jameson, and S. Wille, *J. Phys. Chem.*, 1979, **83**, 3372.

presented by Ramsey.¹³³ The orbital expression consists of two terms, one of which depends only upon the molecular electronic ground state, while the second, in common with the C and D terms, involves a summation over excited electronic states. It has recently been demonstrated that the ground-state orbital term is sufficiently small to be neglected in theoretical considerations of couplings.¹³⁴ In contrast to this the orbital term involving the excited states can account for a significant fraction of the observed couplings in a number of cases, e.g., as large as 67% for $^2J(\text{CH})$ in ethylene.¹³⁵

The inclusion of configuration interaction in MO calculations inevitably leads to a significant increase in the required amount of computer time. A FPT method for evaluating the C term only, involves determining the second derivative of the total energy, thereby rendering the inclusion of configuration interaction a relatively facile process.¹³⁶ The results obtained for some first-row hydrides show that the calculated values of the couplings are reduced by the inclusion of configuration interaction. In order to account for the experimental data it is necessary to include contributions from the O and D terms. For $^1J(\text{FH})$ in HF these non-contact interactions account for about 30% of the observed value.

In general, semi-empirical MO calculations do not account well for geminal couplings. A major reason for this inadequacy lies in the absence of electron correlation effects in such calculations.¹³⁷ Electron correlation has been introduced into some relocalized INDO functions by means of a double perturbation technique.¹³⁸ The contact contribution to spin coupling is represented as the sum of local and non-local contributions. For the geminal couplings of a series of methyl derivatives the local contributions are fairly constant and negative in sign. In contrast, the positive non-local terms appear to be sensitive to substitution. Changes in the central atom, or its bonding arrangement, produces variations in both the local and non-local contributions.

A relativistic theory¹³⁹ has been applied to the calculation of $^1J(\text{CdC})$ and its anisotropy in $\text{Cd}(\text{CH}_3)_2$. Compared with non-relativistic results an increase of 34% in the value of $^1J(\text{CdC})$ is estimated. The comparable increase for the anisotropy is 44%. By comparison with some analogous results on $\text{Hg}(\text{CH}_3)_2$ it appears that the difference in the coupling anisotropies for these two molecules has a relativistic origin.

At the semi-empirical level INDO parameters are usually employed in conjunction with either the FPT or SOS procedure. The resulting expressions for the contact term show that it depends upon *s* electron distribution whereas the non-contact terms relate to *p* electron functions for the first-row nuclei and to *p* and *d* electron functions for the second-row nuclei.

INDO parameterized FPT calculations have been successful in treating C–C and N–C couplings across single and multiple bonds.^{140,141} The C–C couplings are

¹³³ J. Kowalewski, in 'Progress in NMR Spectroscopy', ed. J. Emsley, J. Feeney, and L. H. Sutcliffe, Pergamon, London, 1977, Vol. 11, p. 1.

¹³⁴ W. S. Lee and J. M. Schulman, *J. Chem. Phys.*, 1979, **70**, 1530.

¹³⁵ W. S. Lee and J. M. Schulman, *J. Am. Chem. Soc.*, 1979, **101**, 3182.

¹³⁶ J. Kowalewski, A. Laaksonen, B. Roos, and P. Siegbahn, *J. Chem. Phys.*, 1979, **71**, 2896.

¹³⁷ E. Hiroike, *J. Chem. Phys.*, 1978, **68**, 5305.

¹³⁸ P. Archirel and C. Barbier, *J. Chim. Phys.*, 1978, **75**, 1003.

¹³⁹ J. Jokisaari, K. Räsänen, L. Lajunen, A. Passoja, and P. Pyykkö, *J. Magn. Reson.*, 1978, **31**, 121.

¹⁴⁰ Tun Khin and G. A. Webb, *Org. Magn. Reson.*, 1979, **12**, 103.

¹⁴¹ Tun Khin and G. A. Webb, *Org. Magn. Reson.*, 1978, **11**, 487.

dominated by the C term. Although not negligible, especially in cases of multiple bonding, the O and D terms largely cancel each other.

For a series of $^1J(\text{N}-\text{C})$ and $^1J(\text{N}\equiv\text{C})$ couplings the calculated results suggest negative values. Whereas the single bond couplings are usually controlled by a large negative C term, those across triple bonds have a positive C term that is over-ruled by large and negative O and D terms. A comparison of some SOS and FPT results for C–C couplings, obtained with INDO parameters, has been reported.¹⁴² For various series of couplings ranging from two to five bonds it appears that the SOS results are closest to the experimental data. It is noted that all of the calculations are rather geometry dependent. In this respect the SOS results are more sensitive than those from the FPT procedure.

SOS calculations, employing INDO parameters, have been performed for some N–N and F–N couplings.^{143,144} The N–N couplings appear to be controlled by the C interaction, which in turn depends upon the nature of the valence shell lone-pair electrons, when they have significant *s* character the lone-pair produces a negative C term, whereas a positive C term corresponds to the lone-pair residing in a *p* orbital. The C term is also largely responsible for deciding the sign and magnitude of F–N couplings. However, couplings over more than one bond have significant O and D contributions in addition to the C interaction. Phosphorus lone-pair electrons are responsible for the sign of geminal P–C couplings. FPT calculations with INDO parameters reveal these couplings to be positive for *syn* and negative for *anti* lone-pair orientations.¹⁴⁵ Couplings between directly bonded phosphorus and carbon atoms are controlled by the O term whereas the D term makes the major contribution to the geminal and vicinal couplings.

Similar calculations on $^1J(\text{SiC})$ show that the C term is dominant in providing good agreement with experimental data on a series of model compounds.¹⁴⁶ For some methyl-substituted phosphorines $^1J(\text{PC})$ is reported to be dominated by the O interaction, whereas the other couplings considered are controlled by the D term.¹⁴⁷ The magnitude of $^1J(\text{PP})$ is determined by the conformational features of these molecules. It appears that *d* electrons do not play an important role in the spin–spin interactions between P and P, P and C, and between Si and C.

Spin Relaxation.—Spin-relaxation rates are a major source of information relating to the molecular dynamics of gases, liquids, and solids. In those cases where the desired information is not available from quadrupolar nuclei, it is necessary to investigate the rather more complex relaxation behaviour of coupled spin- $\frac{1}{2}$ nuclei. Analysis of the contributions arising from a number of possible relaxation mechanisms often proceeds *via* the Redfield relaxation matrix, which is then interpreted in terms of molecular models. However, some of the elements of the Redfield matrix correspond to forbidden transitions. Information on these transitions has recently become available by means of multiple quantum two dimensional n.m.r.¹⁴⁸ An illustration of the use of multiple

¹⁴² Tun Khin and G. A. Webb, *Org. Magn. Reson.*, 1980, **13**, 148.

¹⁴³ Tun Khin and G. A. Webb, *J. Magn. Reson.*, 1979, **33**, 159.

¹⁴⁴ Tun Khin, S. Duangthai, and G. A. Webb, *Org. Magn. Reson.*, 1980, **13**, 240.

¹⁴⁵ V. Galasso, *J. Magn. Reson.*, 1979, **34**, 199.

¹⁴⁶ M. D. Beer and R. Grinter, *J. Magn. Reson.*, 1978, **31**, 187.

¹⁴⁷ V. Galasso, *J. Magn. Reson.*, 1979, **36**, 181.

¹⁴⁸ A. Wokaun and R. R. Ernst, *Mol. Phys.*, 1978, **36**, 317.

quantum transitions in interpreting spin-relaxation data in terms of correlated random fields is presented for a two spin- $\frac{1}{2}$ system with external paramagnetic relaxation.¹⁴⁸

The development and application of multiple pulse n.m.r. has made it necessary to consider relaxation in a periodically irradiated spin system. A general theory to cope with this has been derived.¹⁴⁹ In the presence of chemical exchange, multi-pulse experiments effectively scale down the chemical shifts. A theoretical account deals with the prediction of line shapes of chemically shifted resonances undergoing chemical exchange in a multi-pulse experiment.¹⁵⁰ Good agreement is obtained between the theoretical predictions and those measured for the ^{19}F nucleus in a sample of PFBr_2 that is undergoing exchange.

For a triad of identical spin- $\frac{1}{2}$ nuclei the n.m.r. signal may consist of two components. A consideration of the total magnetization as two irreducible sub-magnetizations reveals that the two components transform as momenta with spin- $\frac{3}{2}$ and spin- $\frac{1}{2}$. If the doublet and quartet transitions coincide in frequency then the observed signal comprises two Lorentzians, which may be resolved directly without encountering the inconvenience of multi-dimensional curve fitting.¹⁵¹ Another development has been the derivation of both transient and steady state expressions for Overhauser studies of the $\text{X}_3\text{-}\{\text{A}\}$ type.¹⁵² In contrast to the more usual $\text{A-}\{\text{X}_3\}$ experiment it appears that conventional interpretations of the NOE overestimate the dipole-dipole interaction between the A and X spins. The analysis of strongly coupled spin systems may be treated by means of perturbation response symmetries.¹⁵³ Simplification of the analysis is achieved as well as an indication of experiments that could exploit these symmetries.

In dealing with basic spin-relaxation theory it is usual to express the magnetic dipolar Hamiltonian in terms of irreducible spherical tensors.¹⁵⁴ Recently a much simpler presentation has appeared.¹⁵⁵ Some applications of this development would be interesting. Experimental results demonstrate that ^{13}C spin-relaxation times can be field dependent. Explanations of this phenomenon involve the postulation of a distribution of correlation times. Physically this implies the presence of an infinite number of axes for rotational diffusion. An alternative explanation requires time-dependent correlation times. These may arise due to a change of molecular shape during nuclear relaxation.¹⁵⁶ An illustration of this proposal is provided by an examination of the field and temperature dependence of the spin-lattice relaxation of the mono-protonated carbon in isopropyl alcohol.

¹⁴⁹ A. J. Vega and R. W. Vaughan, *J. Chem. Phys.*, 1978, **68**, 1958.

¹⁵⁰ A. J. Vega, A. D. English, and W. Mahler, *J. Magn. Reson.*, 1980, **37**, 107.

¹⁵¹ E. Haslinger and R. M. Lynden-Bell, *J. Magn. Reson.*, 1978, **31**, 33.

¹⁵² L. G. Werbelow, *J. Magn. Reson.*, 1979, **34**, 132.

¹⁵³ L. G. Werbelow, G. Pouzard, and A. Thevand, *J. Chim. Phys. Phys. Chim. Biol.*, 1979, **76**, 941.

¹⁵⁴ M. W. Spiess, in 'NMR Basic Principles and Progress', ed. P. Diehl, E. Fluck, and R. Kosfeld, Springer, Berlin, 1978, Vol. 15, p. 1.

¹⁵⁵ B. A. Pettitt, *J. Magn. Reson.*, 1979, **34**, 247.

¹⁵⁶ D. M. Doddrell, D. T. Pegg, M. R. Bendall, and D. M. Thomas, *Chem. Phys. Lett.*, 1979, **63**, 309.