

ZERO FIELD NMR ENTIRELY IN HIGH FIELD: THEORY AND EXPERIMENTAL IMPLEMENTATION

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INTRODUCTION

Since the early days of the development of nuclear magnetic resonance (NMR) spectroscopy, there has been considerable interest in the NMR spectra of solids in the absence of an external dc magnetic field¹⁻¹⁰. One important reason for this interest is the fact that zero field spectra may exhibit much sharper, better resolved resonance lines than conventional high field spectra and therefore may be more readily interpreted in terms of the structure of the material under study. The differences between zero field spectra and high field spectra arise from differences in the effective forms of nuclear spin couplings in zero field and in high field. In high field, the couplings depend on the orientation of the locally-defined axis system, e.g. the molecular orientation or crystal axis orientation, with respect to the external dc field. In zero field, the couplings can not depend on orientation because of the isotropy of space in the absence of external fields. Therefore, when the material under study is not a single crystal and all or many orientations of the local axes are present, high field spectra consist of inhomogeneously broadened, "powder pattern" lines, while zero field spectra may still exhibit sharp, well-resolved lines with splittings that contain

structural information. For the case of isolated pairs of spin-1/2 nuclei coupled by a magnetic dipole-dipole interaction, randomly oriented but with a single internuclear distance, the ideal high field and zero field NMR spectra are shown in Fig. 1.

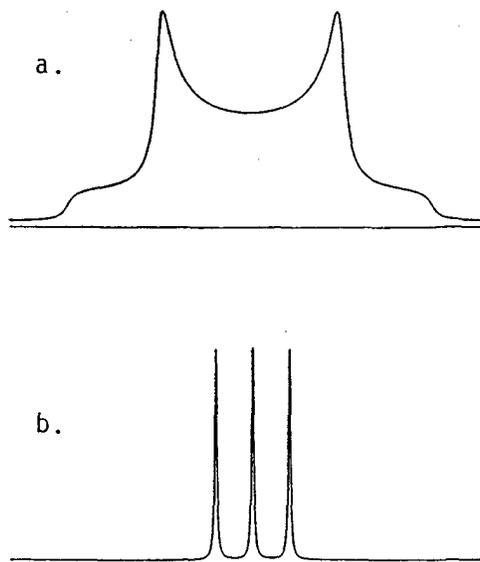


Figure 1: High field (a) and zero field (b) NMR spectra of an ideal system of randomly oriented pairs of spin- $\frac{1}{2}$ nuclei.

There are two substantial difficulties associated with zero field NMR spectroscopy. First, the sensitivity of directly-detected zero field NMR is prohibitively low, particularly for systems of dipole-coupled nuclei or nuclei with small quadrupole couplings. The low sensitivity is due to the low resonant frequencies (0 to 100 kHz) and the small nuclear spin polarizations, or population differences between nuclear spin energy levels, that exist at equilibrium in zero field. Second, it is not generally possible to separate the contributions to the zero field spectrum made by the various elements or isotopes that may be present in the sample of interest. In high field, the various isotopes have their resonant frequencies in distinct, well-separated frequency bands because of their different nuclear magnetic moments. Therefore, one commonly obtains high field NMR spectra of particular isotopes, one at a time. In zero field, however, all nuclei resonate near zero frequency, so that the isotopic selectivity is lost. This lack of selectivity is a significant detriment to studies in which, for example, one would like to determine a molecular conformation by measuring the dipole couplings between isotopic labels introduced at specific sites in a molecule.

Previous approaches to obtaining zero field NMR spectra have overcome the sensitivity problem by using field cycling procedures. In field cycling experiments, samples are polarized in high field and high field signals are detected, but the external field is turned off or the sample is transported out of the field between the polarization and detection periods. The zero field spectrum is obtained indirectly from the modulation of the high field signals as a function of the frequency of audio or rf irradiation applied in zero field¹⁻⁵ (frequency-domain field cycling) or as a function of the time spent in zero field after creation of a non-equilibrium spin state⁶⁻¹⁰

(time-domain field cycling). In principle, field cycling procedures allow zero field NMR spectra to be obtained with the full sensitivity of high field NMR. However, they do not address the problem of isotopic selectivity.

The sensitivity and isotopic selectivity problems could be overcome simultaneously if it were possible to obtain zero field spectra without ever removing the sample from a high field region. At first sight, of course, the notion of zero field NMR entirely in high field seems paradoxical. In this paper, however, we describe a feasible approach¹¹⁻¹³. We show that it is possible, by combining rapid rotation of the sample with the synchronous application of appropriate sequences of resonant rf pulses in high field, to convert nuclear spin couplings from their orientation-dependent, high field forms to orientation-independent, zero field forms. The high field spectra then have the appearance of zero field spectra, but both the sensitivity and the isotopic selectivity of high field NMR are maintained. In addition, because no field cycling is involved, short spin relaxation times do not constitute a limitation on the techniques described in this paper.

In the following sections, the basic theory behind the techniques is reviewed, experimental results are shown, the important experimental non-idealities are described, and potential applications of the techniques are discussed.

THEORY

We have concentrated our efforts on systems of dipole-coupled nuclei, since the dipole couplings in zero field provide a direct measurement of internuclear distances. As is well known, the full magnetic dipole-dipole coupling between a pair of nuclei can be

written in the form

$$H_d = d \sum_{m=-2}^2 (-1)^m Y_{2m} T_{2-m} \quad (1)$$

where $\{Y_{2m}\}$ are second rank spherical harmonics, functions of the angles that specify the orientation of the internuclear vector in space, $\{T_{2m}\}$ is a second rank irreducible tensor operator, a function of the spin angular momentum components of the two nuclei, and d is the coupling constant, proportional to r^{-3} . H_d is the scalar product of the two second rank tensors, meaning that H_d is invariant to simultaneous, equal rotations of the spatial coordinates and the spin angular momenta. As such, H_d can also be written

$$H_d = \sqrt{5} dB_{00} \quad (2)$$

where B_{00} is a zeroth rank tensor, or scalar, under simultaneous rotations of $\{Y_{2m}\}$ and $\{T_{2m}\}$.

In high field, the nuclei experience a Zeeman interaction which is, by definition, much greater than their dipole coupling. Therefore, according to perturbation theory, the only part of H_d that contributes to high field spectra is the part that commutes with the Zeeman interaction, represented by $H_d^{(0)}$. If the applied field is along z ,

$$H_d^{(0)} = dY_{20}T_{20} \quad (3)$$

$H_d^{(0)}$ is clearly not a scalar, leading to the orientation dependence of high field spectra. However, $H_d^{(0)}$ can be rewritten in terms of tensors defined with respect to simultaneous rotations of $\{Y_{2m}\}$ and $\{T_{2m}\}$, with the following result:

$$H_d^{(0)} = d \left(\frac{1}{\sqrt{5}} B_{00} - \frac{2}{\sqrt{14}} B_{20} + \frac{6}{\sqrt{70}} B_{40} \right) \quad (4)$$

In this form, it is apparent that $H_d^{(0)}$ contains a scalar part, which must be proportional to H_d , but it also contains other terms up to and including fourth rank tensors. If these other tensor parts could be eliminated, high field spectra with the appearance of zero field spectra could be obtained.

The elimination of undesired parts of a spin Hamiltonian is by now a highly developed art in NMR, the formal basis of which is provided by coherent averaging theory¹⁴. According to coherent averaging theory, one may attempt to remove the undesired terms from $H_d^{(0)}$ by inducing a periodic time dependence in $H_d^{(0)}$ through some periodic and cyclic experimental manipulations. Provided that the period is small compared to $1/d$ and that NMR signals are observed only at multiples of the period, the spectrum will be determined by the new Hamiltonian $\langle \tilde{H}_d^{(0)}(t) \rangle$, i.e. the average over one period. The experimental manipulations should then be such that

$$\langle \tilde{H}_d^{(0)}(t) \rangle = \sigma H_d \quad (5)$$

in order for the high field spectra to have the appearance of zero field spectra, but with all dipole splittings reduced by the scaling factor σ . Eqs. (2) and (4) imply that the maximum value of σ is $1/5$.

The two types of experimental manipulations that are commonly employed to induce time dependence in spin Hamiltonians in coherent averaging applications are rotation of the sample and irradiation of the nuclei with resonant rf pulse sequences. Sample rotations have the effect of rotating the spherical harmonic Y_{20} in Eq. (3); pulse sequences have the effect of

rotating the tensor operator T_{20} . In order for Eq. (5) to be satisfied with $\sigma \neq 0$, it proves necessary to combine sample rotations and pulse sequences, synchronized in such a way that $\hat{H}_d^{(0)}(t)$ is periodic. The only periodic sample rotations that can be carried out experimentally at present with a sufficiently small period are rotations at a constant angular velocity about a fixed axis, as in magic angle spinning. On the other hand, very intricate pulse sequences, corresponding to very complex rotations of the spin angular momenta, can be applied with rf electronics that are readily available. Within these experimental constraints, several pulse sequence/sample rotation combinations that satisfy Eq. (5) have been found, one of which we discuss in the following section. The method for deriving the pulse sequences will not be discussed here, but has been described previously¹¹⁻¹³.

EXPERIMENTS

Fig. 2 illustrates one of the pulse sequences that we have used to obtain zero field spectra in high field. The sequence has a period of $2\tau_R$, where τ_R is the sample rotation period. In each τ_R period, 20 pulses are applied, occurring as five repetitions of a four-pulse sequence with overall phase shifts of $72^\circ n$, $n = 0,1,2,3,4$. The rf pulse amplitude ν_1 satisfies the condition $\nu_1 = 18.2/\tau_R$. The sample rotation axis is inclined at 66° to the dc magnetic field direction. This sequence has a calculated scaling factor of 0.076.

The sequence in Fig. 2 has two important advantages in practice over sequences that have been described previously. First, the finite amplitude of the rf pulses is explicitly included in the derivation of this sequence; previous sequences were derived with the assumption of infinite rf amplitudes, an assumption that is not justified in

experiments and that leads to reduced resolution in the experimental spectra. Second, the sequence in Fig. 2 has the property that it averages out resonance offsets, anisotropic chemical shifts, and heteronuclear couplings (all of which contribute additional terms to the spin Hamiltonian that are linear in the angular momenta of the spins being observed and that must be averaged out in order for the dipole splittings to be observable) in a period τ_R but creates the desired average dipole coupling in a period $2\tau_R$; previous sequences averaged out the linear terms in a period $2\tau_R$ but created the desired average dipole coupling in a period τ_R . Computer simulations of spectra obtained with various sequences have shown that it is important to average out the linear terms on as rapid a time scale as possible (otherwise distortions of the spectra and poor resolution results), but that the time scale on which the desired average dipole coupling is created can be considerably longer. To further remove the effects of the linear terms, one π pulse is applied and the signs of the rf phases in Fig. 2 are reversed once every $2\tau_R$ period.

Experiments were carried out on selectively deuterated polycrystalline benzene samples. Fig. 3 shows 400 MHz spectra of 1% $C_6H_2D_4/99\%$ C_6D_6 , in which the protons are in meta positions (3a), para positions (3b), and an equal mixture of meta and para (3c). The samples are frozen into roughly spherical shapes in order to reduce magnetic susceptibility broadening. The sample rotation period is 300.0 μs , stabilized to within 0.5 parts per thousand by means of a fiber optical tachometer and feedback circuit to control the N_2 gas pressure to the rotor drive. Tune-up sequences are used to calibrate the rf amplitude and to eliminate rf phase transients. The spectra are obtained in two-dimensional experiments as in reference 12.

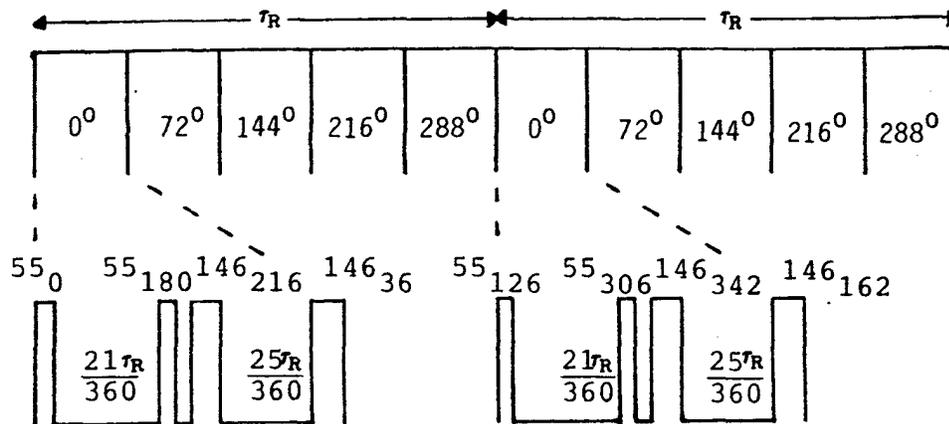


Figure 2: Pulse sequence for obtaining zero field NMR spectra in high field. The sample rotates about an axis inclined at 66° to the applied dc magnetic field.

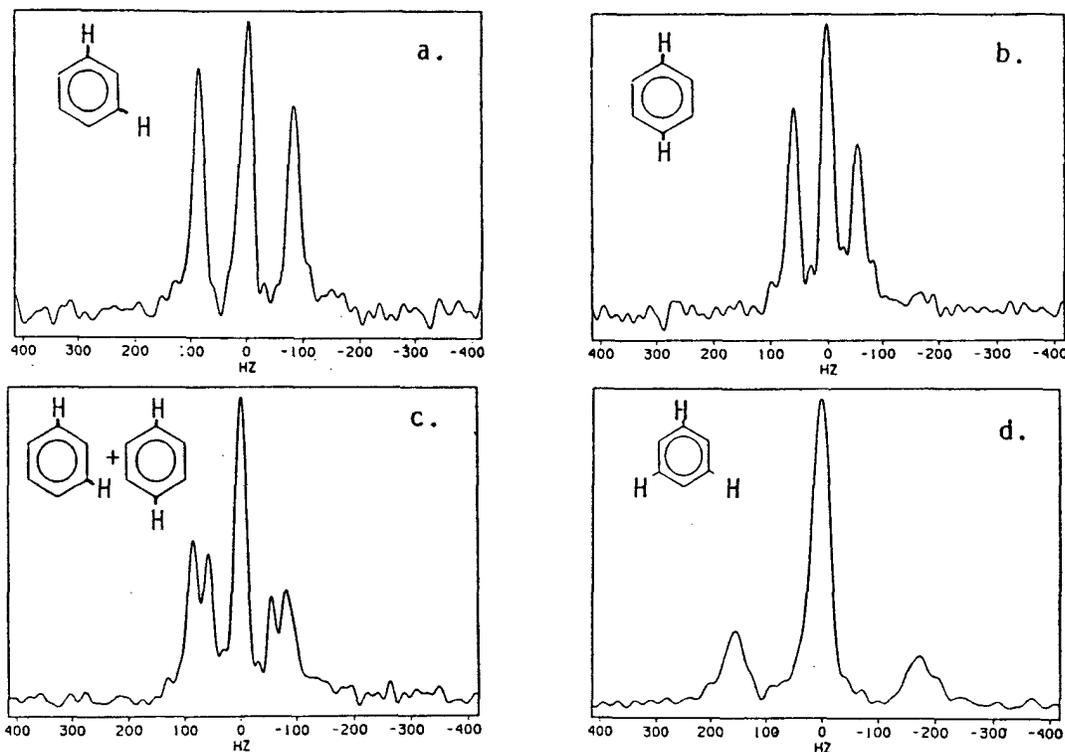


Figure 3: Proton zero field NMR spectra of selectively deuterated polycrystalline benzene samples, obtained in high field using the pulse sequence shown in Fig. 2.

The spectra in Figs. 3a and 3b consist of three equally spaced lines, as expected for the zero field spectra of randomly oriented, isolated pairs of spin-1/2 nuclei with a single internuclear distance. The observed outer splittings of 166 Hz (3a) and 112 Hz (3b) are to be compared with the values 174 Hz and 113 Hz predicted from the known interproton distances (4.29 Å and 4.95 Å) and the calculated σ , taking into account the reduction of the dipole coupling by a factor of two due to rapid rotation of the benzene molecules about their sixfold axes in the solid state. The observed linewidths are about 20 Hz, nearly a factor of two less than the linewidths obtained in previous experiments¹². The improved resolution results from the properties of the pulse sequence described above, the spherical sample shape, and the greater dilution of the protonated molecules.

Fig. 3d is the spectrum of polycrystalline 1% 1,3,5-trideuterobenzene/99% C_6D_6 obtained with the sequence of Fig. 2. As shown in the calculations of Zax et al.⁸, the zero field spectrum in this case of three coupled protons would consist of eleven lines if the molecules were rigid and three lines if the molecules were rapidly rotating. The observation of three lines with a splitting twice as large as in Fig. 3a is in agreement with calculations, demonstrating that zero field spectra of systems of more than two coupled spins can be obtained in high field with the methods described above. This should not be surprising, because the dipole couplings are pairwise interactions and because the pulse sequences are derived using a lowest order coherent averaging approach.

Fig. 4 shows 100 MHz ^{13}C NMR spectra of powdered $Na(CH_3)_2C(OH)SO_3$, in which 5% of the molecules are labelled with ^{13}C in both methyl positions. Fig. 4a is the static, cross-polarized, proton-decoupled spectrum,

showing a powder pattern which is mainly due to chemical shift anisotropy. Fig. 4b is the spectrum obtained with the sequence in Fig. 2 applied to the carbon spins, and with cross-polarization and proton decoupling. In this case, $\tau_R = 400 \mu s$. A spectrum of three lines is again seen as expected, but with substantial distortions due to incomplete averaging out of the anisotropic chemical shift. If a smaller value of τ_R is employed, the chemical shifts are removed more efficiently. However, higher proton decoupling power is also required because the carbon rf amplitude is inversely proportional to τ_R and because the proton rf amplitude must be much larger than the carbon rf amplitude for decoupling to be effective. A proton rf amplitude of 100 kHz was used to obtain the spectrum in Fig. 4b. It is likely that ^{13}C spectra in somewhat lower fields will show better resolution and less distortion due to the smaller absolute values of the chemical shifts.

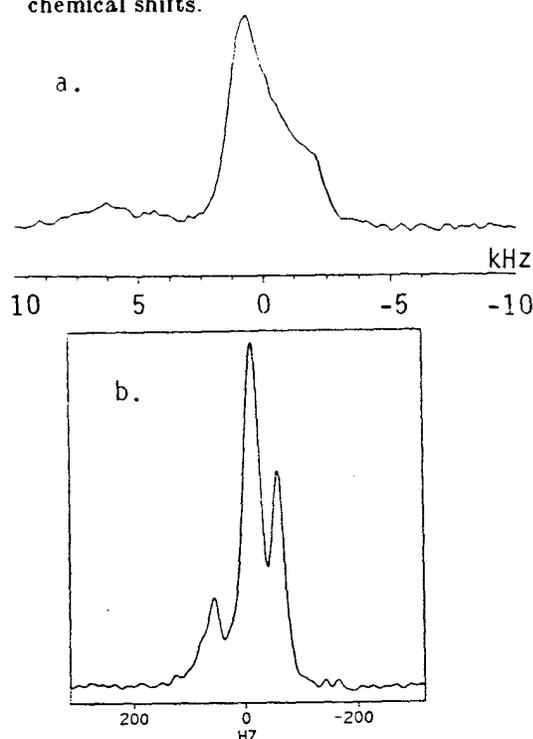


Figure 4: High field (a) and zero field (b) ^{13}C NMR spectra of double-labelled $Na(CH_3)_2C(OH)SO_3$.

CONCLUSIONS

We have demonstrated that it is possible to obtain zero field NMR spectra entirely in high field, thereby maintaining the sensitivity and isotopic selectivity of high field NMR. The proton NMR linewidths of about 20 Hz achieved with the pulse sequence described above, if transferable to other systems of interest, indicate that splittings due to dipole couplings between protons that are up to 10 Å apart can be measured. The corresponding distance for carbons is 4 Å. The ability to measure internuclear distances of this order without requiring single crystal samples suggests that the technique of zero field NMR in high field will prove useful in studies of molecular structures and conformations in polycrystalline and noncrystalline solids. Spectra that consist of sharp lines rather than powder patterns are particularly advantageous in cases where pairs of coupled nuclei with several possible internuclear distances are present and where the distribution of distances is of interest. Such cases include noncrystalline synthetic polymers, where the distribution of internuclear distances may provide information about the distribution of backbone or sidechain conformations, and biopolymers that have been biosynthetically labelled in several positions, e.g. proteins in which particular amino acids or pairs of amino acids are isotopically labelled. Zero field spectra may also prove useful for determining the radial distribution functions of dopants in inorganic glasses and semiconductors. These and related applications are currently being investigated.

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