Developments in Solid-State NMR

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Solid-state NMR is, at once, both intriguing and informative. This article attempts to explain what makes this methodology different from the mainstream NMR and highlights its utility.

1. Introduction

Students, when introduced to nuclear magnetic resonance (NMR), are curious to know why there is a sub-branch within NMR called solid-state NMR. It is pertinent to mention here that a majority of NMR spectra are, in general, recorded in the solution state, meaning that the samples are dissolved in a solvent and then the spectra are recorded. The reason for this is that though the NMR spectrum of a solid sample is intrinsically rich in information, its interpretation poses severe challenges, thus making it unsuitable for routine use. However, a number of interesting chemical and biological systems need to be investigated in the solid state and at high resolution. Examples of such systems are solid-state catalysts, polymers, membranes, large and insoluble proteins, liquid crystals and a variety of inorganic materials. In view of this, it becomes imperative to understand the reasons that hamper the routine use of NMR spectroscopy in the solid state and ways to overcome these limitations. It might be interesting to learn that the difference between the spectra of samples in the solid state and the liquid (or solution) state arises due to the presence or the absence of ‘anisotropy’.

To understand anisotropy, imagine schoolchildren standing in rows for the morning prayer as shown in Figure 1a. For the teacher of the class, it is much easier to move along the rows than across the rows. This may

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be termed as motional or velocity anisotropy. This is the situation one obtains in solids. Most of the properties of materials in the solid state, such as electrical conductivity, refractive index, etc., are anisotropic and the magnitude of the relevant parameter estimated is dependent on the direction of measurement with respect to the crystal axes. In the case of NMR also, the resonance frequency of the nuclear spin in the externally applied magnetic field in the solid state is direction dependent. To understand this, we should recall that the NMR resonance frequency depends not only on the external magnetic field but also on local factors such as the electronic cloud around the nucleus and the presence of other nuclear spins in the vicinity, etc., whose distribution, in general, is anisotropic. The consequence of this is that the NMR resonance frequency of the nucleus depends on how the solid crystal is placed in a magnetic field. For different orientations of the crystal in the magnetic field, the resonance frequencies are different.

In contrast, in the liquid state, a situation akin to what is shown in Figure 1b with the group of children after the prayer class occurs. Once they are free, the children are randomly distributed and also move randomly in all directions. In this case, the teacher will have equal amount of difficulty in moving in any direction and this
is an example of velocity ‘isotropy’. A similar situation occurs in liquids where molecules execute rapid and random translational and rotational motion. As a consequence, the material properties also become isotropic and independent of the direction of measurement. In NMR, the anisotropic part of the local factors (or interactions) averaged over time due to molecular motions become zero, leaving only the direction independent isotropic part. It also turns out that some of the local interactions of the nucleus which exert their influence in the spectra recorded in the solid state, have a zero isotropic average. Thus, in solution, interactions such as nuclear dipole–dipole interaction and nuclear quadrupolar interactions do not affect the spectral line positions. They however can have an effect on the intensity and the width of the resonance lines through relaxation. The absence of these interaction in the liquid state is an advantage in the sense that the spectrum shows the effect of only chemical shifts and J-couplings which have non-zero isotropic part and is relatively easy to interpret. In contrast, an NMR spectrum in the solid state is complex due to the presence of all the interactions along with their anisotropy.

2. Interactions in the Solid State

Electrons orbiting around the nucleus as well as those involved in bonding with neighbouring atoms produce a magnetic field at the site of the nucleus, as a result of which the resonance frequency of the nucleus shifts away from that of a bare nucleus. This shift is known as the chemical shift and the position of the resonance line of a nucleus among a group of lines acts as a fingerprint of the chemical environment of the nucleus.

Information gathered from all such lines in the spectrum leads to the unravelling of the structure of the molecule. In the solid state, the anisotropy of chemical shift (referred to as chemical shift anisotropy or CSA)
causes the position of the resonance line to shift according to the orientation of the molecule. In a powder sample which contains a large number of tiny, randomly-oriented crystals, individual molecular orientation is also random with equal probability for all directions. This results in a continuum of resonance frequencies over a range. The spectrum is therefore an overlap of a large number of very closely spaced lines and appears to the eye as a broad single resonance line. An illustration of the influence of this interaction is shown in Figure 2a. For a molecule containing many distinct chemical sites, the broad lines of each of these sites overlap with one another and produce an overall spectrum which is very complex to analyze.

In the solid state, in addition to chemical shift, the nuclear dipole–dipole and the nuclear quadrupole interactions also become important. The nuclear spin is a magnetic dipole. Hence it can interact with magnetic dipoles of other nuclei. This interaction is called the direct dipole–dipole (or simply dipolar) interaction. This is different from the interaction between nuclear spins through the electron cloud which is referred to as the indirect spin–spin interaction or the J-coupling interaction.

The J-coupling is generally small and in the solid state, it is mostly neglected in comparison to other interactions which are larger by orders of magnitude. The dipolar
interaction causes the resonance line to split with the frequency separation between the split lines providing a measure of the distance between the nuclear spins. Again, the dipolar interaction is anisotropic. The magnitude of the splitting depends on the angle between the vector connecting the two nuclei and the magnetic field. As in the case of CSA broadening mentioned above, for a powder sample, this results in broadened line shapes (Figure 2b). The dipolar coupling has a $\frac{1}{r^3}$ dependence and it is a through-space interaction. As a consequence of this, a nuclear spin can dipolar-couple to several other nuclear spins and the dipolar broadened line is a composite line-shape arising out of all such dipolar couplings a nuclear spin has with its neighbours.

In the early stages of the development of NMR, such linear shapes, particularly of protons, were used for studying the structure of solids, on set of phase transitions, etc. Also, methods to get rid of the dipolar coupling (called decoupling) were developed, keeping particularly in mind, protons which are ubiquitous in organic solids. The purpose of decoupling protons is that, with the dipolar couplings to protons removed, the effect of other interactions, such as the chemical shift interaction on the nuclear spins can be observed. The dipolar interaction can be further classified as that between similar spins (as between one proton and another proton in the molecule) called homonuclear dipolar interaction and that between dissimilar spins (say between a proton and a carbon) called heteronuclear dipolar interaction. There is a reason why these two interactions are different. The broad line due to heteronuclear dipolar coupling can be viewed, like a CSA broadened line, as the overlap of several pairs of dipolar doublets. This is called an inhomogeneously broadened line. In the case of lines broadened due to homonuclear dipolar coupling, it is incorrect to view the broadened line as superposition of several lines. This is because homonuclear spins have nearly the same
resonance frequency. Consequently, they can easily exchange their energy with coupled neighbors.

An up→down transition of one spin is balanced by a corresponding down→up transition of its neighbor. Hence perturbations caused to spins giving rise to resonances in one part of the spectrum are transmitted to the entire spin system. The broad spectrum of the entire group of spins behaves as if it is the natural line-width of the nuclei. Such a broadening is referred to as homogenous broadening. This property of the homonuclear spins has both an advantage and a disadvantage. The advantage is that the whole group of spins can be manipulated by electromagnetic irradiation at any part of the spectrum. In the past, this property for example, was utilized for simultaneously decoupling all protons together from their coupled carbon nuclei by relatively low-power RF irradiation at a single frequency in the center of the proton spectrum known as CW decoupling. A carbon spectrum recorded under this condition has a simple appearance due to the removal of the proton–carbon dipolar couplings. The major disadvantage with homonuclear dipolar coupling arises during the observation of the homonuclear species themselves. For example, observation of chemical shift of an individual proton chemical site after getting rid of its dipolar coupling to other protons is a problem that has not found a completely satisfactory solution even today.

Another interaction that manifests in the spectra in the solid state is the nuclear electric quadrupole interaction. Nuclei having a spin \( I = 1/2 \) have a spherical distribution of electric charge. But nuclei with \( I > 1/2 \) have a non-spherical charge distribution, which gives rise to the electric quadrupole moment. Such nuclei can sense the gradient in the electric field (EFG) produced by the surrounding electrons and can have orientations with different energies. This interaction can also affect the
energies of the nuclear spin states as shown in Figure 3a for a spin \( I = 3/2 \). The electric quadrupole interaction (also called simply as quadrupolar interaction) and specified by the quantity \( \omega_q \), the quadrupole coupling constant, can have a wide range of magnitudes depending on the nucleus under consideration and the electric field gradient (EFG) at the site of the nucleus. Thus, deuterium with \( I = 1 \) typically has an \( \omega_q \sim 250 \) kHz, whereas chlorine (\(^{35}\)Cl) has \( \omega_q \) of about 35 MHz. Depending on the magnitude of \( \omega_q \) in comparison to that of the nuclear resonance frequency \( \omega_0 \), the quadrupolar interaction can be classified as first order and second order. For a spin \( I = 3/2 \) as seen in the Figure 3a, there are four energy levels corresponding to magnetic quantum number, \( m = -3/2, -1/2, +1/2 \) and \(+3/2\). There are three transitions possible, namely \(+3/2\rightarrow+1/2\), \(+1/2\rightarrow-1/2\) and \(-1/2\rightarrow-3/2\). In the absence of the quadrupolar interaction (which can happen if the atom occupies a site having cubic or higher symmetry with EFG equal to zero), all the transitions have the same energy and the three spectral lines overlap at the same frequency. But for \( \omega_q \) small but not equal to zero, the energy levels shift as shown in Figure 3a, due to the first order effect. The \(+1/2\rightarrow-1/2\) transitions frequency remains unchanged. This is called the central transition. The frequencies of the \(+3/2\rightarrow+1/2\) and \(-1/2\rightarrow-3/2\) are modified and one spectral line appears on either side of the central transition. These are called the satellite

![Figure 3. (a) Energy levels and transitions corresponding to a spin \( I = 3/2 \) nucleus. Three cases corresponding to zero, small (1st order) and large (2nd order) quadrupole coupling constants (qcc) are depicted. (b)\(^{11}\)B NMR spectrum showing the central transitions of borax recorded with magic angle spinning. Of the two chemically-distinct boron sites, the left peak shows 2nd order broadening due to a larger qcc. The sharp right side peak corresponds to boron with a negligible qcc. The satellite peaks are not visible due to very low intensity. Courtesy: R V Sudheer Kumar, PhD thesis, IISc, Bangalore](image-url)
transitions. If $\omega_q$ becomes large, then, the second order effects start to appear and this affects the position of the central transition also which had remained unaffected in the first order. What is depicted in the Figure 3a is for a single nucleus. In a powder sample, one observes the quadrupolar powder pattern. The satellite transitions are affected by both the first order and second order interactions. Very often, they become so broad that they lose intensity and hence are not observed. The central transition for a powder sample is sharp for small values of $\omega_q$. For large values of $\omega_q$, due to second order effects, the line broadens (Figure 3b). One should remember that these lines will show in addition, the effects of isotropic and anisotropic chemical shifts and dipolar interactions to the neighbouring nuclei. While all the above interactions contain valuable information about the material under investigation, the challenge is to resolve the influence of each one of them on the spectrum and extract the relevant information. A major part of the developments in the area of NMR of the solid state has been concerned with how to get rid of the line broadening effect due to various interactions and resolve spectral lines corresponding to different chemical sites.

3. High Resolution Spectra in the Solid State

From the discussion in the preceding section, it is apparent that NMR spectra in the solid state are intrinsically broad. It was recognized in the early days of NMR that it is necessary to obtain spectra with high resolution comparable to what is available for the solution-state. Towards this end, a two-pronged approach was initiated based on the general characteristics of the interactions that cause the broadening of the NMR spectrum. The Hamiltonian $\mathcal{H}$ corresponding to these interactions can be written in a general form as

$$\mathcal{H} = k A T^{-1}$$  \hspace{1cm} (1)
where $A$ is the space-part and $T$ contains the spin variables. For example, the heteronuclear dipolar Hamiltonian representing the dipolar interaction between two spins $I$ and $S$ can be written as

$$H_{IS} = k_I \frac{\gamma_I \gamma_S}{r_{IS}^3} \times \frac{(3 \cos^2 \beta - 1)}{2} \times 2I_ZS_Z,$$  

where $\gamma_I$ and $\gamma_S$ are the gyromagnetic ratios of spin $I$ and spin $S$ respectively, $r_{IS}$ is the distance between the two nuclear spins, $I_Z$ and $S_Z$ are the components of the respective spin-vectors along the direction of the external magnetic field applied along the $Z$-direction and $\beta$ is the angle between the inter-nuclear vector $r_{IS}$ and the magnetic field $B_0$. Since the $I$ and $S$ spins belong to two different atoms, $r_{IS}$ represents the inter-atomic distance and $\beta$ is the angle between $r_{IS}$ and $B_0$. If a solid sample is rotated in a magnetic field, it is easy to see that the angle $\beta$ changes.

One may also note that physically rotating the sample does not have an effect on the spin vectors $I$ and $S$. This is equivalent to what we observe in a compass where the magnetic needle always points towards the north in whatever way we hold the compass. The direction of the compass needle can however be changed if we bring another magnet nearby. In a similar fashion, the orientation of the spin vectors can be changed by introducing a magnetic interaction, say by the magnetic field component of the electro-magnetic radiation that we use in NMR. Thus it is possible to independently change the space part of the Hamiltonians in (1) and (2) by a physical rotation of the sample, while the spin components can be altered by the application of radio-frequency radiation near the resonance frequency of the nuclear spins.

The method to obtain high-resolution spectrum in the solid state is to get rid of the anisotropic part of the interactions that produce broadening by making the rele-
vant part of the Hamiltonians of the type shown in (1) and (2) to zero. This is achieved by changing the Hamiltonians in a periodic fashion such that the average of the Hamiltonian over the time period is zero. There are two ways of doing this – by manipulating either the space part $A$ or the spin part $T$ of the Hamiltonian. It may be noticed in (2) that the Hamiltonian becomes zero for $\beta = 54.7^0$. Some of the other interactions discussed earlier can also be reduced to a similar form. This fact has been utilized in the method known as magic angle spinning (MAS), where the sample kept in a small sample holder called the rotor, is spun rapidly about an axis making an angle 54.7$^0$ with respect to the magnetic field direction (Figure 4). Such a rotation ensures that all inter-nuclear vectors $r_{IS}$ in (2) have, on the average, an angle 54.7$^0$ which is called the magic angle $^\beta_M$. As a consequence of this rotation, interactions such as the heteronuclear dipolar, chemical shift anisotropy and first order quadrupolar interactions average to zero. Homonuclear dipolar coupling among protons is removed by radio-frequency irradiation. Using this method of magic angle spinning combined with high-power proton decoupling, high-resolution spectra for spin $\frac{1}{2}$ nuclei such as $^{13}$C, $^{31}$P, $^{15}$N are obtained. Some of the quadrupolar nuclei such as $^7$Li, $^{11}$B and $^{27}$Al have relatively small quadrupolar coupling. Spectra of such nuclei are also obtained with the MAS technique. Some examples of this are shown in the Figures 3 and 4.
As mentioned earlier, homonuclear dipolar interaction has a different behaviour and consequently it is not easily amenable to magic angle spinning.

As a means of obtaining proton chemical shifts while proton homonuclear dipolar coupling are removed, manipulation of the spin terms of the Hamiltonian of (1) with radio-frequency (RF) pulses was proposed and the method known as ‘multiple pulse decoupling’, was developed by John Waugh (Figure 5) who has made pioneering contributions for the development of solid-state NMR. In this approach, the nuclear spin vectors are rendered time dependent using RF irradiation. The time average of the homonuclear dipolar Hamiltonian in the first order is rendered zero while other interaction terms can be retained partially. For studying protons, a better method was later evolved which combined MAS and decoupling called CRAMPS (combined rotation and multiple pulse decoupling). Increasing the speed of the spinning of the sample in MAS is being currently explored. However, achieving resolution of proton spectra in the solid state comparable to those available in solution still remains an enigma. Some examples of proton spectra obtained in the solid state are illustrated in Figure 6.

**Figure 5.** John S Waugh. Professor, MIT (1929–2014)

**Figure 6.** Proton spectra of L-Histidine. HCl.H₂O recorded with
(a) MAS frequency of 20 kHz and with multiple pulse decoupling,
(b) MAS frequency of 55 kHz and
(c) MAS frequency of 20 kHz. Courtesy: Y Jayasubba Reddy, PhD thesis, IISc, Bangalore.
Modern Developments and Conclusion

For a long time, NMR spectroscopists were concerned with simplifying the spectra in the solid state and increasing resolution. In the process of increasing resolution, valuable information that is contained in the anisotropic part of the interactions was getting lost. For example, the chemical shift anisotropy and the dipolar couplings are parameters that provide highly useful structural and dynamics information. Therefore, even as attempts to enhance resolution were in progress, there were attempts to recover the information that had been lost. Such experiments that are designed to recover information lost due to say, magic angle spinning, are called ‘recoupling’ experiments. In terms of NMR instrumentation, solid-state NMR is much more demanding in comparison to solution-state NMR.

This pertains to factors such as the ability to spin samples at a high speed combined with spinning-speed stability, ability to produce high power RF pulses with near ideal characteristics of frequency, phase and amplitude stability and so on. Recent developments in these areas and development of a large number of standard experiments has made solid-state NMR a routine analytical method. Like NMR in the solution state, a plethora of

![Figure 7](image)

Figure 7. Proton 2D-NMR spectra of L-Histidine.HCl.H₂O in the solid state. (a) Proton-carbon chemical shift correlation spectrum. (b) Proton double-quantum shift carbon chemical shift correlation spectrum.

two-dimensional NMR experiments have also been developed (*Figure 7*). With all this progress, high-resolution solid-state NMR promises to be a powerful technique for investigating a variety of systems.

**Suggested Reading**
