Multiple Quantum Spectroscopy[*]

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I. Introduction

The aim of this paper is to give a non-specialist some familiarity with a novel technique in pulsed NMR called Multiple Quantum Spectroscopy. Despite its recent institution there is now a vast amount of literature on the subject dealing with a diversity of problems in liquids, liquid crystals and solids as well. The method is elegant and turns out to be powerful in structural, conformational and motional studies, yet it is rather simple in principle. These features are undoubtedly responsible for its overwhelming success.

This paper is not meant as a review of the literature, but rather as an introduction to the subject and to stimulate the reader to read the original papers. A rather complete reference to the literature on multiple quantum spectroscopy covering also the historial aspects is given in a recent review article by Bodenhausen (1). In the present paper we limit ourselves to

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the modern versatile pulse version pioneered by the groups of Hashi (2), Pines (3) and Ernst (4).

Multiple quantum NMR spectroscopy deals with the preparation, evolution and detection of multiple quantum coherences; i.e., phase relationships (1), between any two states differing in Zeeman quantum numbers by $\Delta M = m$. In the ordinary single quantum spectroscopy only coherences between states satisfying the selection rule $\Delta M = \pm 1$ are dealt with. It thus follows that multiple quantum NMR has an advantage over the single quantum NMR as it offers all the information obtainable by NMR. Specifically the higher quantum subspectra are usually better resolved and easier to interpret than the single quantum spectrum. For example, the single quantum spectrum of oriented benzene has 76 lines (5), whereas the five-quantum and six-quantum spectra have only two lines and one line, respectively (6,7). In N dipolar coupled spin $\frac{1}{2}$ systems the N-1 and N-2 quantum subspectra are usually sufficient to determine all dipolar couplings (8). In studies of molecular motions the multiple quantum relaxations provide information not accessible by the single quantum relaxation

studies (9,10). Finally, in some experiments, such as the Jeener-Broekaert pulse sequence for measuring the dipolar relaxation in solids, multiple quantum effects are generated (11) which interfer with the measured quantity. Therefore knowledge of multiple quantum spectroscopy is indispensable to avoid making errors in pulsed NMR.

II. Principles

The general method of Pulsed Fourier Transform Multiple Quantum Spectroscopy (PFT-MQS) is as follows. First the multiple quantum coherences are prepared. Next the coherences are allowed to evolve in time. Subsequently the evolution is detected with the help of a detection pulse. The multiple quantum spectrum is obtained by a Fourier transform of the evolution. A typical pulse sequence is depicted in Figure 1 where multiple quantum coherences are prepared by applying two rf pulses P_1 and P_2 timed τ apart (τ^{-1} is typically of the order of the strength of the spin-spin interaction) to the spin system initially in equilibrium. After an evolution time t_1, during which the multiple quantum free induction decay (MQ-FID) takes place, a detection pulse P_3 is applied to transform the invisible multiple quantum coherences into an observable single quantum coherence. This is called the indirect detection. It is similar to the detection by a 90° pulse in relaxation measurements. The transverse magnetization signal $S(t_1)$ either sampled as a single time point or as a whole decay after $t_2 \geq \tau$ (the latter is done for enhancing the signal to noise ratio) is observed as a function of t_1. Observing S as a function of t_1 is crucial in this procedure, but τ and t_2 can be fixed. The whole pulse sequence is repeated with incremented t_1-values. The evolution of the multiple quantum coherences mapped out on S as a function of t_1 can be Fourier transformed to obtain the multiple quantum spectrum. This procedure is not strictly necessary, however.

In order to understand the above we refer to a few well established formula. The behavior of the spin system, say with total spin j, can be easily understood by expanding the density matrix into a complete set of irreducible tensor operators T^l_m of orders $l \leq 2j$, with m satisfying the relation $-l \leq m \leq l$ (12,13):

$$\rho(t) = 1 - \Sigma_{l,m,n} C_{l,m,n}(t) \, T^l_{m,n} , \quad (1)$$

where n numbers the occurrence of T^l_m and m denotes m-quantum coherence which is present when $C_{l,m,n}(t) \neq 0$. We note that $1 = T^0_0$ is included to form the complete set; see Section III for a simple example.

An rf pulse P_i rotates T^l_m as follows (13):

$$P_i T^l_m P_i^{-1} = \Sigma_{m'} T^l_{m'} D^l_{m'm} , \quad (2)$$

where $D^l_{m'm}$ is the Wigner rotation matrix. We assume that the Hamiltonian H of the spin system, in a frame rotating at angular frequency ω of the rf pulses, is of the form:

$$H = \Delta I_z + H_{cs} + H_{ss} \quad (3)$$

where ω_0 is the Larmor frequency, $\Delta = \omega_0 - \omega$ the resonance offset, H_{cs} the chemical shift interaction and H_{ss} is a bilinear spin-spin interaction. H_{ss} could be a scalar interaction in liquids, a dipolar, or a quadrupolar interaction in liquid crystals and solids. It is essential for generating the multiple quantum coherences to have such a bilinear interaction. This interaction can be truncated in high fields $[H_{ss}, I_z] = 0$.

Between the pulses the spin system evolves as determined by the Hamiltonian of equation 3. T^l_m is then transformed into $T^{l'}_m$ of all orders $l' \leq 2j$. The quantum number m is conserved, however (12-14).

$$\exp(iHt) T^l_m \exp(-iHt) =$$

$$\Sigma_{l'} A_{ll'm}(t) T^{l'}_m . \quad (4)$$

In many techniques to distinguish between different multiple quantum

orders the following is employed:

$$\exp(i\alpha I_z) T'_m \exp(-i\alpha I_z) =$$

$$T'_m \exp(im\alpha) \qquad (5)$$

which readily follows from equation 5-66b of reference (13). In practice α may be a phase shift (6,15), frequency (or field) offset (6,11) or a field gradient (16). It follows that multiple quantum coherences can be created by successive applications of equations 2 and 4. With the initial condition

$$\rho(0) = 1 - \beta T^1_0, \qquad (6)$$

where $T^1_0 = I_z$ (Zeeman order), at least two rf pulses are needed to prepare multiple quantum coherences. Such a set is the pulse sequence in Figure 1. However, with the initial condition

$$\rho(0) = 1 - \beta T^2_0, \qquad (7)$$

where $T^2_0 = H_{ss}$ (dipolar order in solids), a single $90°$ pulse selects double quantum coherence (17).

Since m quantum coherence for $m \neq \pm$

1 is not observable, a detection pulse is needed to rotate T'_m into $T'_{\pm 1}$, see equation 2. This becomes the observable $T^1_{\pm 1}(= \mp I_{\pm})$ after a time $t_2 \geq \tau$; see equation 4. The whole procedure is summarized in Figure 1. The above analysis follows closely that given in reference (18). Also reference (6) should be read.

III. Examples

We discuss some simple techniques for obtaining multiple quantum spectra using the three-pulse method. In practice P_1, P_2 and P_3 can be either all equal, say all $90°_x$ pulses, or all different pulses. In Figure 2 the energy level scheme of protons in the rapidly reorienting CH_3 or NH_3^+ group oriented in a nematic liquid crystal or in a solid is given; d is the effective static part of the intramolecular dipole-dipole interaction. The energy levels are classified according to the A $(I = 3/2)$, $E^a(I = 1/2)$ and $E^b(I = 1/2)$ irreducible representations of the point group C_3 (19).

In terms of T'_m, a complete set for the spin system of A symmetry
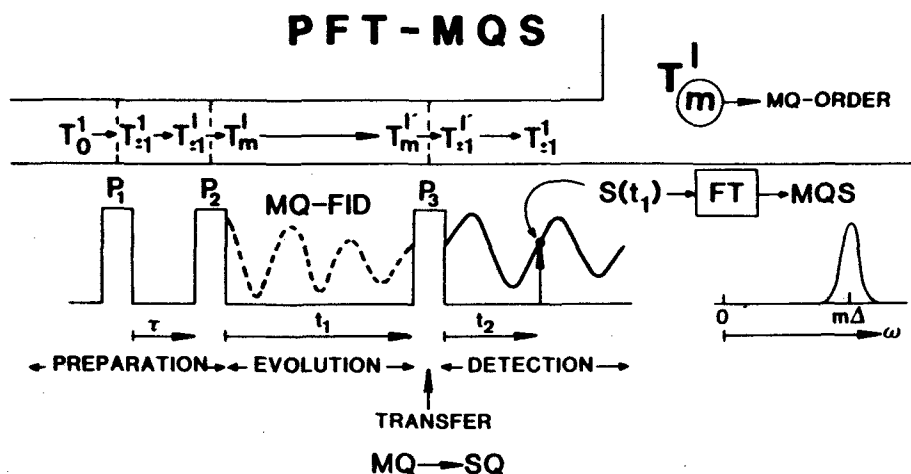

Figure 1. Preparation, evolution and detection of multiple quantum coherences by the three-pulse method.

is formed by $\{1, T^1_m, T^2_m, T^3_m\}$ having 16 components altogether. A complete set for the spin 1/2 system of E^a or E^b symmetry is formed by $\{1, T^1_m\}$ having in total 4 components.
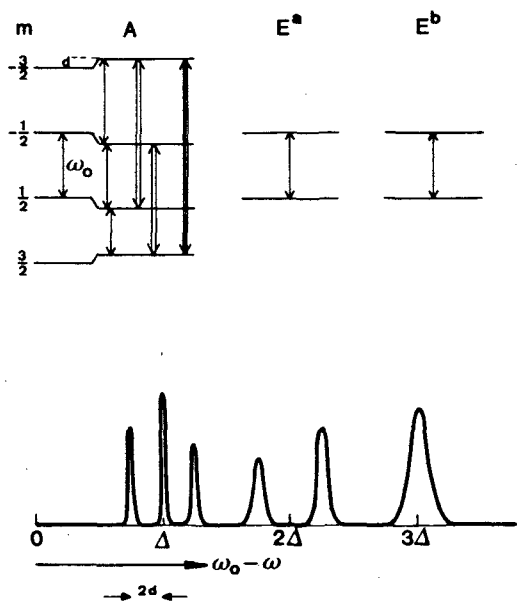

Figure 2. The proton energy level scheme and the multiple quantum spectrum of rapidly reorienting CH_3 (or NH_3^+) groups in nematic intensity ratio's are unlike ordinary single quantum spectrum.

In this example T^1_m appears 3 times; this illustrates the meaning of n in equation 1. The explicit forms of the T'_m in terms of I_z, I_+ and I_- are given in Table 1 (20). The single, double and triple quantum coherences are denoted by arrows with single, double and triple bars in Figure 2 and the corresponding subspectra are centered around Δ, 2Δ, and 3Δ, respectively, where Δ is the offset frequency. It should be noted that the intensities are functions of Δ, d, and τ. Their ratio's are not as in the ordinary single quantum spectrum and the subspectra need not be symmetric.

The use of an offset (3,6,11) to distinguish the different multiple quantum orders is simple indeed. However, unfortunately the broadenings due to field inhomogeneity of the lines also are proportional to the order. In solid (11,17) where the field inhomogeneity broadening is negligible compared to the dipolar line width, this is not a problem, but in high resolution spectra of liquids (4) and of liquid crystals (6-8) the field inhomogeneity broadening may be limiting the linewidth. This inhomogeneity broadening can be removed by applying a 180° pulse in the middle of the evolution period, however in this case the offset is also removed from the evolution. An ingenious time proportional phase increment (TPPI) method (6) restores an apparent offset in the following way. In addition to the 180° pulse the multiple quantum coherences are rotated about the z-axis, see equation 5, by a rotation angle α which is made proportional to the incremented t_1:

$$\alpha = \Delta \, t_1 \quad , \qquad (8)$$

where Δ is the apparent offset. The experiment can be done on resonance, which has the advantage that the sampling frequency during t_2 is lower than with an offset, see Figure 1. The rotation about the z-axis was achieved by shifting the rf pulses with a phase shifter, but it can be done also by a sequence (21), since

$$\exp(i\pi I_x/2) \exp(i\alpha I_y) (-i\pi I_x/2) =$$

$$\exp(i\alpha I_z) \qquad (9)$$

without the need for a phase shifter. The TPPI method is extensively used by Pines' group to obtain spectra in liquid crystalline solvents without broadening due to the field inhomogeneity. Phase shifting has also been used to detect certain orders selectively (11,15,17). To see this in a simple manner, consider equation 5 for $\alpha = 0°$ and $\alpha = 180°$. If we add both signals the odd quantum contributions disappear, if we subtract them the even

quantum contributions disappear.

Another simple method to detect multiple quantum orders selectively is to use strong pulsed field gradients. These dephase the multiple quantum coherences proportional to the order when applied during the evolution period and only the zero quantum coherences ($m = 0$) are unaffected. When a detection pulse is applied the zero quantum coherences are transformed into single quantum coherences, see equation 2, and can be observed (15). Since zero quantum coherences are insensitive to magnetic field inhomogeneity one can get a narrow line zero quantum spectrum even in very inhomogeneous magnets; see however the remark in reference (1) on this aspect. The pulsed field gradient method was extended (16) to the selective observation of each' order by adding another pulsed field gradient in the detection period to refocus the transformed multiple quantum coherences. Since these transformed coherences evolve as single quantum coherences after the detection pulse, the pulse width of the refocusing field gradient should be taken proportional to m to exactly refocus only the m quantum coherences and so detect the m quantum order selectively. Furthermore, to avoid interference with the zero quantum coherences which also transforms into single quantum coherences, the refocusing field gradient is applied shortly after the detection pulse to destroy the signal from zero quantum coherences.

Finally we mention techniques for wideband selective excitation of multiple quantum coherences. While the selective detection is rather simple to do, the selective excitation requires a good deal of expertise and wit, except in special cases (17). The general method is by no means simple (7,22-25). Only the selective double quantum excitation (17) is easy to interpret. In this case one first prepares a dipolar state, see equation 7. A $90°$ pulse rotates T^2_0 into $T^2_{\pm 2}$ and T^2_0 only, thus selectively creating double quantum coherence.

IV. Applications

It was argued in many papers on the subject and also mentioned in the introduction that simplicity and better resolution make the interpretation easier in high quantum spectra. Indeed, multiple quantum spectroscopy turns out to be a powerful tool in structural and conformational (8,26), as well as in relaxation (9-11, 27-28) studies.

The analysis of the biphenyl conformation in a liquid crystal in the nematic phase (8) demonstrates that multiple quantum spectroscopy is a better alternative to the more elaborate and time-consuming selective isotopic substitution method. The detection of $^{13}C - ^{13}C$ scalar coupled pairs in liquid samples (with natural ^{13}C abundance) by the double quantum coherence which is present in the coupled spin pairs and absent in uncoupled spins is another example of its utility (26). Multiple quantum spectroscopy is useful also in relaxation studies since it provides additional information about the parameters of motion (9,10,28). It is also able to resolve the quantity of interest from interference effects (11). That the knowledge of multiple quantum spectroscopy is needed to understand pulsed NMR was demonstrated in dipolar relaxation (29,30).

V. Prospects

Unlike many new techniques in NMR we consider multiple quantum spectroscopy as "total" NMR. The various techniques known in the single quantum NMR can be extended to multiple quantum spectroscopy, as already indicated in the various applications. Recently multiple quantum decoupling (31), double quantum cross-polarization (32), multiple quantum double resonance (33), multiple pulse multiple quantum spectroscopy (34) were introduced. In the future a multiple quantum zeugmatography may be important. I believe that multiple quantum NMR will be a major topic in NMR in the years to come and may have impact also in other fields, such as optics (35).

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