FORMULATION AND ANALYSIS OF TWO-PULSE PHASE MODULATION BASED HETERONUCLEAR DIPOLAR DECOUPLING SEQUENCES IN NMR

by

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Certificate

I certify that the thesis entitled ***Formulation and Analysis of Two-Pulse Phase Modulation Based Heteronuclear Dipolar Decoupling Sequences in NMR*** submitted by Cyril Augustine to Indian Institute of Technology New Delhi, for the award of the degree of Doctor of Philosophy is a record of bona fide research work done by him. He has worked under my guidance and supervision and has fulfilled the requirements for the submission of this thesis which to my knowledge has reached the requisite standard. The results presented in this thesis have not been submitted in part or full to any other University or Institute for the award of any other degree or diploma.

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Slowly the night grows and light diminishes from the shadows of creeping wine branches,
half-slept in the cradle song of winter.
This night, it departs from me like dark horses with its usual speed.
It does not stop for me, oh God. This is the winter of my life.
This is the blossom of my apple trees which was reluctant to arrive.
Farewell, I bid farewell to you, my dearest Campus.
Farewell, I bid farewell to you Delhi, the old city of ruined dynasties.
After many years, an old man may come back from the vales of the Koorg Hills,
to find the lost bells, his memories and his old NMR laboratory.

Cyril Augustine

Abstract

Heteronuclear dipolar decoupling is an essential requirement for extracting structural information from the ^{13}C NMR spectra of liquid crystals and solids. There are many effective heteronuclear dipolar decoupling schemes for the study of these systems. Nevertheless there is a continuous quest for better decoupling schemes that still persists in the literature. In this thesis some decoupling schemes for heteronuclear dipolar decoupling in liquid crystals and solids are formulated and compared with other commonly used decoupling sequences.

Some efficient decoupling schemes for heteronuclear dipolar decoupling in liquid crystals are formulated by supercycling SW_f-TPPM, a sequence introduced recently for rotating solids. The parent SW_f-TPPM sequence is considered as R and a supercycle is constructed in the form of $R\ R\ \bar{R}\ \bar{R}$, where $\bar{R}$ implies the phase inverted counterpart of R. This decoupling sequence is denoted as SW_f-$TPPM_{11}S$. The relative intensities of the aliphatic α, β, γ, and δ carbons in the decoupled ^{13}C spectra of the liquid crystal 4-n-pentyl-4'-cyanobiphenyl (5CB) are considered and a comparison is made between SW_f-$TPPM_{11}S$ and some commonly used heteronuclear dipolar decoupling schemes in anisotropic liquids namely, SPINAL-64 and the parent SW_f-TPPM. The effectiveness of the decoupling programme with respect to experimental parameters such as RF field strength, decoupler offset frequency and phase angle is also analyzed. Similarly, a shorter SW_f-TPPM based decoupling scheme, denoted by SW_f-$TPPM_7$ is also generated and supercycled. This is represented by SW_f-$TPPM_7$. The overall performance of SW_f-$TPPM_7S$ is inferior to the supercycled version of SW_f-$TPPM_{11}$, but it may become useful when a sequence with a shorter cycle time is required.

Later, the performance of the supercycled SW_f-TPPM for heteronuclear dipolar decoupling in solid samples is studied with respect to variation of three experimental parameters;

the phase angle, proton offset, and the MAS frequency. The supercycled version of SW_f-TPPM was applied in a standard sample of U-^{13}C-labelled tyrosine for heteronuclear dipolar decoupling between ^{13}C and ^{1}H and its efficiency of decoupling is compared with the other commonly used decoupling sequences in solids such as SPINAL-64 and the parent SW_f-TPPM. The supercycled version of SW_f-TPPM gives relatively good enhancement in the intensity of all the decoupled peaks. Intensity gain for the decoupled resonances is one of the desirable features for a good decoupling scheme. However, the sequence should also be sturdy in performance with respect to various experimental parameters such as the offset of the RF irradiation, pulse phase angle and RF field strength. Thus, one of the decoupled peaks from the aliphatic region is selected (CH_2 carbon, at 36 ppm) and analyzed as a function of proton offset for SPINAL-64, SW_f-TPPM and SW_f-TPPMS decoupling. As the proton off-resonance value increases, the efficiency of SW_f-TPPMS scheme remains relatively unaffected. Also, the results of varying phase angles from 10° to 40°, with an increment of 5°, on the intensities of the decoupled CH_2 peak is analyzed at a constant MAS frequency. It is observed that an optimum phase angle of 15° gives better decoupling for both SW_f-TPPM and its supercycled version. The efficiency of decoupling at larger phase angles deteriorates in both cases, but the supercycled sequence still shows relative enhancement in the intensities of the decoupled peaks.

Also, numerical simulations are done to compare the efficiency of the parent SW_f-TPPM and its supercycled version for heteronuclear dipolar decoupling in solids using the SIMPSON program. The selected spin system is a ^{13}C nucleus dipolar-coupled to two protons. Both the heteronuclear and homonuclear dipolar couplings are considered in the simulations and the calculations are done at different MAS frequencies (6, 8 and 14 kHz), phase angles (15 to 40°) and RF field strengths (80 to 160 kHz). The results of simulations and experiments are

compared. Simulations also show that the supercycled SW_f-TPPM is better than its parent version in the low RF power region of 80-100 kHz, at the MAS frequencies ranging from 15 to 25 kHz.

Unlike anisotropic liquids and solids, where both dipole-dipole and *J*-coupling prevail, systems of isotropic liquids show only *J*-coupling because the secular parts of the intramolecular and intermolecular dipole-dipole couplings average to zero due to rapid motion of the molecules in the isotropic systems. The TPPM and SW_f-TPPM family of sequences are originally developed for heteronuclear decoupling in solid state NMR. Although the underlying principles of decoupling in isotropic and anisotropic systems are different, it would be interesting to ascertain the behavior of these decoupling sequences in isotropic liquids and to understand their efficiency in removing scalar heteronuclear interactions. The spin dynamics during these sequences can be explored easily in the liquid state because of the smaller interaction strengths and the absence of many body effects. Thus, the performance of TPPM based sequences in isotropic spin systems is revisited with regard to the experimental parameters, phase angle and decoupler offset. A comparison is made with other commonly used heteronuclear decoupling schemes in liquids, namely WALTZ-16, GARP and MLEV. Also, the trajectories of nuclear magnetization vector of abundant nuclei in a simple spin system during TPPM and SW_f-TPPM decoupling sequences are traced out using computer simulations. The results indicate that decoupling sequences designed specifically for liquid state applications outperform the TPPM and SW_f-TPPM sequences. This is an expected result because TPPM and its variants are designed for decoupling in solids where heteronuclear dipolar couplings dominate.

The pulse durations given in SW_f-TPPM follow a tangential sweep. It is possible to formulate new variants with less number of TPPM blocks maintaining a tangential increase in

the pulse length. In this manner, a shorter sequence is designed called SW_f-TPPM-4, which contain 4 TPPM blocks. There are four pulse pairs in this sequence and their pulse lengths vary from 0.82τ to 1.18τ. The SW_f-TPPM-4 sequence can be represented as, $\{[0.82\tau_\varphi\ 0.82\tau_{-\varphi}]\ [0.98\tau_\varphi\ 0.98\tau_{-\varphi}]\ [1.02\tau_\varphi\ 1.02\tau_{-\varphi}]\ [1.18\tau_\varphi\ 1.18\tau_{-\varphi}]\}$. Even though SW_f-TPPM-4 is a shorter sequence in comparison with SW_f-TPPM it still maintains a reasonable tangential sweep in the pulse durations. In the second stage, a phase incremental alteration is applied in this sequence to form two basic elements Q and $\overline{Q}$, where $Q = [0.82\tau_{10}\ 0.82\tau_{-10}]\ [0.98\tau_{15}\ 0.98\tau_{-15}]\ [1.02\tau_{20}\ 1.02\tau_{-20}]\ [1.18\tau_{15}\ 1.18\tau_{-15}]\}$ and $\overline{Q} = [0.82\tau_{-10}\ 0.82\tau_{10}]\ [0.98\tau_{-15}\ 0.98\tau_{15}]\ [1.02\tau_{-20}\ 1.02\tau_{20}]\ [1.18\tau_{-15}\ 1.18\tau_{15}]\}$. Later Q and $\overline{Q}$ are supercycled to form a series of sequences called PHINTAPT-16 = $Q\overline{Q}$, PHINTAPT-32 = $Q\overline{Q}\overline{Q}Q$, and PHINTAPT-64 = $Q\overline{Q}\overline{Q}Q\quad\overline{Q}Q\overline{Q}Q$. Here the name PHINTAPT implies decoupling sequences with **PH**ase angle **IN**crements and **TA**ngential variation in **P**ulse **T**imes.

Two of the resulting decoupling schemes PHINTAPT-32 and PHINTAPT-64 are compared with other two commonly used decoupling sequences in solids and liquid crystals namely, SPINAL-64 and SW_f-TPPM by comparing the intensities of selected resonances in the proton decoupled ^{13}C spectrum of U-^{13}C-labelled tyrosine and the liquid crystal 4-n-pentyl-4'-cyanobiphenyl (5CB). A systematic comparison is presented with respect to the experimental parameters such as RF field strength, MAS frequency and proton offset frequency. These sequences provide appreciable improvement in decoupling performance over SPINAL-64 and SW_f-TPPM schemes as proved by experiments.

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