Novel Methods for Improving Resolution in Liquid and Solid State Nuclear Magnetic Resonance Spectroscopy

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UNIVERSITY OF MIAMI

NOVEL METHODS FOR IMPROVING RESOLUTION IN LIQUID AND SOLID
STATE NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

By

Lauren Fae O’Donnell

A DISSERTATION

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NOVEL METHODS FOR IMPROVING RESOLUTION IN LIQUID AND SOLID
STATE NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

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NMR spectroscopy is a versatile analytical platform with a well developed theoretical foundation that makes it a popular vehicle for biological, chemical, material, and medical research. Successfully deciphering an NMR spectrum in order to extract important structural and chemical information typically requires the separation of overlapping signals that can be limited by the available spectral resolution, which is itself influenced by numerous factors such as molecular motions, spin-spin couplings, and field inhomogeneities.

In this dissertation, methods for improving spectral resolution in both liquid and solids are explored. To begin, a brief introduction to NMR theory is provided which includes an introduction to quantum mechanical treatments of spin systems, an overview of Average Hamiltonian Theory and description of Walls’s method for designing pathway selective pulses, PSPs. In Chapter two, the reverse INEPT pathway selective pulse, or RIPSP, is presented and shown to generate a pure rotation of an \( I \) spin (e.g., \(^1\text{H}\)) only for nonzero heteronuclear coupling to an \( S \) spin (e.g., \(^{13}\text{C}\)) in \( I_nS \) spin systems. When the RIPSP is applied to more complex systems, such as \(^{13}\text{C}\) labeled sugars, it was shown that line narrowing occurred. The origin of this line narrowing is explored in Chapter three. A theory is proposed that the
line sharpening is due to the contribution from multispin, single-quantum coherence coupled with correlated $B_1$ and $B_0$ field inhomogeneities.

In Chapter four, focus is turned to the study of spin-$\frac{1}{2}$ dipolar solids where line narrowing under a CPMG or $\pi$-pulse train is explored. A theory is developed that shows $\pi$-pulse imperfections in a CPMG pulse train generate an effective “pulsed” spin-locking of single-quantum coherences with phase $^+(\phi_x \phi_y)$. Long-lived signals and line narrowing were observed in experiments on both magnetically dilute, random spin networks, such as those found in $C_{60}$ and $C_{70}$, and in adamantane and ferrocene samples.
To see the world for a moment as something rich and strange is the private reward of many a discovery.

-Edward M. Purcell, Nobel Lecture

December 11, 1952
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Finally, I would like to express the joy and comfort that I have felt in caring for my cat, Eris, over the last 16 years.

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CHAPTER 1

Introduction

The first successful NMR experiments were performed in December of 1945 by Felix Bloch [1] and in January of 1946 by Edward Purcell [2] and his group. Both men subsequently shared the Nobel Prize in physics for their work in 1952 [3, 4]. At the time of his Nobel Lecture, Purcell had already described many theoretical aspects of NMR in detail [2–4], providing the foundation upon which experiments can be developed with insight toward projected outcomes given the theoretical framework. Since the 1950s NMR has become a popular tool in research across multiple disciplines. This popularity has driven development of both technology and technique in magnetic resonance as researchers seek sharper spectral resolution. On the technology front, there exists a vast array of specialty probes which can be tailored for working with all manner of materials at various temperature and pressure. Further technological work has also improved both the strength and homogeneity of the magnetic field, from the 0.1 Tesla electromagnet used by Bloch in 1945 to superconducting magnets with field strengths exceeding 28.2 Tesla [5]. In addition to advances in hardware, the simplicity of the spin interactions and the relatively long coherence times in nuclear spin systems have ushered in a variety of pulse sequences that can be used to control spin dynamics in order to simplify spectra.

One of the main research directions in the area of NMR has focused on developing methods to improve resolution. In this dissertation, new pulse sequences are developed that are shown to improve spectral resolution in both solid and liquid state systems. Since these systems rely of the nuances of NMR theory, the basic theoreti-
cal foundations are provided in Chapter 1. First, an overview of density matrices are provided, followed by a discussion of the basic interactions that contribute to the nuclear spin Hamiltonian. This is then followed by an overview of average Hamiltonian theory whereby radiofrequency (RF) pulses can manipulate the intrinsic Hamiltonian such that the nuclear spin system effectively evolves over the pulse sequence. This chapter is concluded by an application of Walls’s method of Pathway Selective Pulse (PSP) design [6]. In Chapter 2, a presentation of a PSP based upon the reverse INEPT sequence, referred to as the RIPSP, is shown to selectively excite on those protons coupled to a $^{13}$C spin. In Chapter 3, it is shown that the RIPSP can also generate line narrowing in multispin systems. In Chapter 4, the application of $\pi$-pulse trains in solid-state systems, such as adamantane, ferrocene, C$_{60}$ and C$_{70}$ is shown to generate line narrowing.

1.1 The Density Matrix

Density matrix theory is a concise method for describing quantum dynamic systems such as those under complex NMR experiments [7,8]. This technique effectively simplifies the system by averaging the isolated spin states contained within the sample into an ensemble representation used for statistical mixtures called the density operator. The density operator can be represented by a matrix where the elements contained therein provide comprehensive information regarding physically relevant variables of the system [8,9].

1.1.1 Definition of the Density Matrix

The density matrix in quantum mechanics has a function similar to the distribution function in classical statistical mechanics applied to group symmetric operations over some defined $n$-dimensional vector space [8–10]. A consequence of the uncertainty principal states that physical observables yielded through experimentation cannot be measured with precision simultaneously, but if two operators, $\hat{X}_1$ and $\hat{X}_2$, commute
it is possible to find states for which the corresponding eigenvalues, $x_1$ and $x_2$, are defined. The most complete characterization of a system is made when all of the eigenvalues corresponding to the maximum number of possible commuting observables have been measured by experiment. Such a system may then be specified by a state vector for each eigenvalue, $|x_n\rangle$, of the desired observables $\chi_n$, where measurement of observable $\chi_n$ over the state $|x_n\rangle$ returns the expected eigenvalue $x_n$ [8]. If there exists two sets of observables, $\{\chi : \chi_1, \chi_2, \ldots, \chi_n\}$ and $\{\chi' : \chi'_1, \chi'_2, \ldots, \chi'_n\}$ with eigenstates $|\psi\rangle = |x_1, x_2, \ldots, x_n\rangle$ and $|\phi\rangle = |x'_1, x'_2, \ldots, x'_n\rangle$ in which at least one of the operators $\hat{\chi}'$ does not commute with set $\chi$, the state $|\psi\rangle$ can be written as a linear superposition of $n$ eigenstates of $|\phi\rangle$:

$$|\psi\rangle = \sum_n c_n |\phi_n\rangle$$

and the adjoint state is defined as

$$\langle \psi | = \sum_n c^*_n \langle \phi_n |$$

In this representation, the states $|\phi_n\rangle$ comprise the set of basis states where $|\psi\rangle$ is written in the basis $\{\phi\}$. The correspondence between states $|\psi\rangle \rightarrow |\phi\rangle$ defines an operation between the vector sets [10]. These basis states are said to be orthonormal if the condition,

$$\langle \phi_n | \phi_m \rangle = \delta_{nm}$$

is met where the definition of orthonormality is; $\{v_i, i = 1, 2 \ldots\}$ when $\langle v_i | v_j \rangle = \delta_{ij}$. The $\delta_{ij}$ here is the Kronecker Delta defined as;

$$\delta_{ij} = \begin{cases} 1 & i = j \\ 0 & i \neq j \end{cases}$$

1.1.2 Characteristics of the Density Matrix

The density matrix can be used to derive any physical variable through the choice of operator used to obtain corresponding expectation values as the initial parame-
ters for a system. The following properties of the density matrix are presented for clarification.

(I) The density operator, $\hat{\rho}$, is Hermitian and meets the condition

$$\langle \phi_i | \hat{\rho} | \phi_j \rangle = \langle \phi_j | \hat{\rho} | \phi_i \rangle^*$$  \hspace{1cm} (1.5)

(II) The diagonal elements of $\rho$ represent the probability of finding the system in a specific state. The equation

$$\rho_{mm} = \sum_n W_n |c^n_m|^2$$  \hspace{1cm} (1.6)

indicates that because the probability of finding $|\psi_n\rangle$ in state $|\phi_m\rangle$ is $|c^n_m|^2$ and the probability that the system is in state $|\psi_n\rangle$ is $W_n$, then the diagonal element of $\rho_{mm}$ is the probability of finding the system in state $|\phi_m\rangle$. This relation indicates that $\rho_{mm} \geq 0$, a sensible conclusion given that a probability will not be less than 0.

(III) After a measurement is made to the system, the probability of finding the system in state $|\psi\rangle$ is given by $W(\psi) = \langle \rho | \psi \rangle$.

(IV) The trace of $\rho$ is constant regardless of the representation. This condition is argued as follows,

$$\text{Tr} \rho = \sum_i \rho_{ii} = \sum_a W_a \sum_n |c^n_i|^2 = 1$$  \hspace{1cm} (1.7)

(V) The trace of the product of $\rho$ and any operator $\hat{\chi}$, returns the expectation value $\chi$.

$$\langle \chi \rangle = \sum_{mm'} \sum_n W_n c^n_m c^{n*}_{m'} \langle \phi_m | \hat{\chi} | \phi_{m'} \rangle$$  \hspace{1cm} (1.8)

$$= \sum_{mm'} \langle \phi_{m'} | \rho | \phi_m \rangle \langle \phi_m | \hat{\chi} | \phi_{m'} \rangle$$  \hspace{1cm} (1.9)

$$= \text{Tr} \{ \rho \hat{\chi} \}$$  \hspace{1cm} (1.10)
1.1.3 The Density Matrix for a Quantum System in Thermal Equilibrium

Consider an $n$-dimensional quantum system that is in thermal equilibrium with a lattice at temperature $T$. For such a system, the thermal equilibrium density matrix, $\hat{\rho}_0$, is given by:

$$
\hat{\rho}_0 = \frac{\exp\left(-\frac{\hat{H}}{k_B T}\right)}{\text{Tr}\left\{\exp\left(-\frac{\hat{H}}{k_B T}\right)\right\}}
$$

(1.11)

where $k_B$ is Boltzmann’s constant, and $k_B T$ is referred to as the thermal energy. If \(\{\Phi\} = \{\vert \phi_1 \rangle, \vert \phi_2 \rangle, \ldots, \vert \phi_n \rangle\}\) represents an eigenbasis for $\hat{H}$ with $\hat{H} \vert \phi_m \rangle = E_m \vert \phi_m \rangle$, then

$$
\hat{\rho}_0 = \sum_{k=1}^{n} e^{-\frac{E_k}{k_B T}} \vert \phi_k \rangle \langle \phi_k \vert
$$

(1.12)

where $p_m = \langle \phi_m \vert \hat{\rho}_0 \vert \phi_m \rangle = \frac{e^{-\frac{E_m}{k_B T}}}{\sum_{k=1}^{n} e^{-\frac{E_k}{k_B T}}}$ represents the probability for a system at thermal equilibrium to be in state $\vert \phi_m \rangle$.

It follows that the relative probabilities between two states $\vert \phi_m \rangle$ and $\vert \phi_j \rangle$ is given by:

$$
\frac{p_m}{p_j} = \exp\left(\frac{E_j - E_m}{k_B T}\right) = \exp\left(\frac{\Delta E_{jm}}{k_B T}\right)
$$

(1.13)

As an example, consider the simple case of a 2-dimensional system, such as a spin $I = \frac{1}{2}$, with states and corresponding energies given by $\vert \alpha \rangle$ (spin-up along the $+\hat{z}$-direction) and $\vert \beta \rangle$ (spin-down along the $-\hat{z}$-direction) and $E_\alpha$ and $E_\beta$, respectively. In this case, $\hat{\rho}_0$ is given by:

$$
\hat{\rho}_0 = \frac{e^{-\frac{E_\alpha}{k_B T}} \vert \alpha \rangle \langle \alpha \vert + e^{-\frac{E_\beta}{k_B T}} \vert \beta \rangle \langle \beta \vert}{e^{-\frac{E_\alpha}{k_B T}} + e^{-\frac{E_\beta}{k_B T}}}
$$

$$
= \frac{1}{2} (\vert \alpha \rangle \langle \alpha \vert + \vert \beta \rangle \langle \beta \vert) + \frac{\tanh\left(\frac{\Delta E_{\beta\alpha}}{2k_B T}\right)}{2} (\vert \alpha \rangle \langle \alpha \vert - \vert \beta \rangle \langle \beta \vert)
$$

$$
= \frac{1}{2} \mathbf{1} + \text{pol.} \hat{I}_Z
$$

(1.14)
where $\hat{1}$ is the $2 \times 2$ identity matrix, and $\hat{I}_Z$ is the $z$-component of the spin angular momentum operator, and $\text{pol.} = \tanh \left( \frac{\Delta E_{\beta\alpha}}{2k_B T} \right)$ is the spin polarization which represents the difference in probabilities between being an up-spin and a down-spin. If $|\Delta E_{\beta\alpha}| \gg k_B T$, then $\text{pol.} \approx 1$ and the spins are nearly 100 percent polarized in the $|\alpha\rangle$ spin state. However, if $|\Delta E_{\beta\alpha}| \ll k_B T$ (which is the situation encountered in most NMR studies), then $\text{pol.} \ll 1$. Under the condition $|\Delta E_{\beta\alpha}| \ll k_B T$, often referred to as high temperature conditions, $\hat{\rho}$ can be approximated as:

$$\hat{\rho}_0 \approx \frac{1}{2} \hat{1} + \frac{\Delta E_{\beta\alpha}}{2k_B T} \hat{I}_Z$$

$$= \frac{1}{2} \hat{1} + \hat{\rho}_{\text{eq,red.}}.$$

(1.15)

where $\hat{\rho}_{\text{eq,red.}}$ is the reduced density matrix and represents the deviation for a completely unpolarized spin system (in this case, the $\hat{z}$-magnetization generated by an energy difference between up and down spins). It is $\hat{\rho}_{\text{eq,red.}}$ that is affected RF pulses and contributes to the observed signal in an NMR experiment.

### 1.2 Interactions in NMR

The Hamiltonian $\hat{H}$ essentially determines, not only the dynamics of a quantum system, but also the initial equilibrium density matrix. Therefore, in this section the basic interactions of an ensemble of spins over the course of an NMR experiment are described. The Hamiltonian can be represented by a sum of various interaction Hamiltonians [17, 18]. The dominant interactions in the NMR of solids and liquids is the Zeeman interaction, which is basically the interaction of the nuclear spin with the large, static magnetic field. This interaction governs the initial equilibrium polarizations and the basic frequencies at which RF pulses are applied, and where the detection coils are tuned for observation. However, the interesting interactions that provide unique spectroscopic fingerprints of molecules are related to chemical shift and scalar spin-spin or “J-coupling” in liquids, and the dipole-dipole interactions and chemical shift anisotropy in solid-state systems (since this work focuses on $^1H$ and $^{13}C$
NMR experiments, the quadrupolar interaction, which is relevant for spins greater than $I > \frac{1}{2}$, will not be discussed. Before introducing the basic interactions in NMR, a brief mathematical tutorial will be presented on matrices, product operators, and tensors.

Consider a set of equivalent spins - $(\frac{1}{2})$ that do not interact with one another. If these spins are placed in a strong magnetic field in which they become oriented along the z-axis, two state vectors can be assigned: $|x\rangle = +\frac{1}{2}$ or $|x\rangle = -\frac{1}{2}$. When $|x\rangle = +\frac{1}{2}$ they are all described as ‘spin-up’ and their associated state vector is represented as

$$|+\frac{1}{2}\rangle = \begin{bmatrix} 1 \\ 0 \end{bmatrix} \quad (1.16)$$

Similarly, when $|x\rangle = -\frac{1}{2}$ the spins are all described as ‘spin-down’ and their associated vector represented as

$$|-\frac{1}{2}\rangle = \begin{bmatrix} 0 \\ 1 \end{bmatrix} \quad (1.17)$$

Consider a collection of $I = \frac{1}{2}$ spins that do not interact with one another. In the following, we will show how to construct the relevant product operators that can describe the Liouville space in which the density matrix evolves. To begin, consider a single spin $I = \frac{1}{2}$. As mentioned above, the two spin states are $|\alpha\rangle \equiv |\frac{1}{2}\rangle$ and $|\beta\rangle \equiv |-\frac{1}{2}\rangle$. We can represent these states (and their corresponding adjoint states) as a vector as follows:

$$\Psi_1 = \psi_1 = |\alpha\alpha\rangle \quad (1.18)$$

$$\Psi_2 = \psi_2 = |\alpha\beta\rangle \quad (1.19)$$

$$\Psi_3 = \psi_3 = |\beta\alpha\rangle \quad (1.20)$$

$$\Psi_4 = \psi_4 = |\beta\beta\rangle \quad (1.21)$$

For a single spin, the dimension of the Liouville space is simply $2^2 = 4$, which means that an arbitrary density matrix for a single spin can be represented as a linear
combination of four, linearly independent operators. One common basis is a spin operator basis given by the Pauli Matrices:

\[
\begin{align*}
\hat{\sigma}_0 &= \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}, \\
\hat{\sigma}_x &= \begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix}, \\
\hat{\sigma}_y &= \begin{bmatrix} 0 & -i \\ -i & 0 \end{bmatrix}, \\
\hat{\sigma}_z &= \begin{bmatrix} 1 & 0 \\ 0 & -1 \end{bmatrix}
\end{align*}
\] (1.22)

\[
(A_x)_n^k = \langle \psi_n | \hat{A}_x | \psi_k \rangle
\] (1.23)

In this case, an arbitrary density matrix can be written as:

\[
\hat{\rho} = \begin{bmatrix} a & c^* \\ c & b \end{bmatrix} = \frac{a + b}{2} I + (a - b) \hat{I}_Z + (c + c^*) \hat{I}_X + \frac{c - c^*}{i} \hat{I}_Y
\]

\[
= \lambda_1 \hat{I} + \lambda_{i_z} \hat{I}_Z + \lambda_{i_y} \hat{I}_Y + \lambda_{i_x} \hat{I}_X
\] (1.24)

where \( \lambda_\hat{O} \) is the coefficient of operator \( \hat{O} \) which can be calculated by:

\[
\lambda_\hat{O} = \frac{\text{Tr} \left[ \hat{O}^\dagger \hat{\rho} \right]}{\text{Tr} \left[ \hat{O}^\dagger \hat{O} \right]}
\] (1.25)

The direct product of two arbitrary matrices \( \hat{B} \) and \( \hat{D} \) is denoted by \( \hat{C} = \hat{B} \otimes \hat{D} \): Calculating each element for the \( \hat{A}_x \) matrix for a two spin AX system gives the matrix representation for \( \hat{A}_x \):

\[
\hat{A}_x = \begin{bmatrix} 0 & 0 & 1/2 & 0 \\ 0 & 0 & 0 & 1/2 \\ 1/2 & 0 & 0 & 0 \\ 0 & 1/2 & 0 & 0 \end{bmatrix}
\] (1.26)

The direct product is given by \( \hat{C} = \hat{B} \otimes \hat{D} \) where \( \hat{B} \) and \( \hat{D} \) are arbitrary matrices and \( \hat{C} \) is the resultant matrix product. Invoking the group theoretical definition from Tung [10], Let \( B \) and \( D \) be subgroups of \( C \) such that \( b_m \in B \) commutes with any element of \( d_n \in D \) and every element \( c_k \in C \) can be written uniquely as \( c = b_m d_n \) then \( C \) is said to be the direct product of \( B \) and \( D \). In NMR, spin system interactions
are vector spaces that are direct products of other vector spaces resulting from the degrees of freedom within the system.

\[
\hat{C} = \hat{B} \otimes \hat{D} = \begin{bmatrix}
B_{11} \hat{D} & B_{12} \hat{D} & \ldots & B_{1m} \hat{D} \\
B_{21} \hat{D} & B_{22} \hat{D} & \ldots & B_{2m} \hat{D} \\
B_{31} \hat{D} & B_{32} \hat{D} & \ldots & B_{3m} \hat{D} \\
\vdots & \vdots & \ddots & \vdots \\
\vdots & \vdots & \ddots & \vdots \\
B_{m1} \hat{D} & B_{m2} \hat{D} & \ldots & B_{mm} \hat{D}
\end{bmatrix}
\] (1.27)

applying this for \( \hat{A}_x \) gives

\[
\hat{A}_x = \hat{\sigma}_x \otimes \hat{\sigma}_0 = \frac{1}{2} \begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix} \otimes \frac{1}{2} \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}
\] (1.28)

There are \( 2^{2N} \) square basis matrices of dimension \( 2^N \) for a system of \( N \frac{1}{2} \) spins and all of these matrices may be expressed as direct products of the single spin Pauli matrices, \( \hat{\sigma}_x, \hat{\sigma}_y, \hat{\sigma}_z \) and the unit matrix, \( \hat{\sigma}_0 \). These basis matrices form a complete set and from them all other matrices for the system can be constructed from linear combinations of them. For example, a two spin-\( \frac{1}{2} \) system will have \( 16 \cdot (4 \times 4) \) basis matrices. Each of these 16 matrices describes a measurable spin configuration of the system deriving from the associated products of the individual spin matrices.

The associated matrix operators for a two spin system of \( I = \frac{1}{2} \) are referred to as product operators of the system. The single spin operators for a two spin system are given by:
The remaining 9 operators, \( \hat{I}_Z \hat{I}_Z \), \( \hat{I}_X \hat{I}_X \), \( \hat{I}_Y \hat{I}_Y \), \( \hat{I}_Z \hat{I}_Z \), \( \hat{I}_X \hat{I}_X \), \( \hat{I}_Z \hat{I}_Z \), \( \hat{I}_X \hat{I}_X \), \( \hat{I}_Z \hat{I}_Z \), and \( \hat{I}_Y \hat{I}_Y \) can be found by simply multiplying together the corresponding matrices in Eq. (1.29). For example,

\[
\hat{I}_{X1} = \hat{I}_X \otimes \hat{I}_Z = \frac{1}{2} \begin{bmatrix}
0 & 0 & 1 & 0 \\
0 & 0 & 0 & 1 \\
1 & 0 & 0 & 0 \\
0 & 1 & 0 & 0
\end{bmatrix}, \quad \hat{I}_{Y1} = \hat{I}_Y \otimes \hat{I}_Z = \frac{i}{2} \begin{bmatrix}
0 & 0 & -1 & 0 \\
0 & 0 & 0 & -1 \\
1 & 0 & 0 & 0 \\
0 & 1 & 0 & 0
\end{bmatrix},
\]

\[
\hat{I}_{Z1} = \hat{I}_Z \otimes \hat{I}_X = \frac{1}{2} \begin{bmatrix}
1 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 \\
0 & 0 & 1 & 0 \\
0 & 0 & 0 & 1
\end{bmatrix}, \quad \hat{I}_{Y2} = \hat{I}_Y \otimes \hat{I}_X = \frac{i}{2} \begin{bmatrix}
0 & 1 & 0 & 0 \\
1 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 \\
0 & 0 & 0 & 1
\end{bmatrix}.
\]

The resulting matrices can be combined as

\[
\hat{I}_{X1} \hat{I}_{Y2} = \frac{i}{4} \begin{bmatrix}
0 & 0 & 1 & 0 \\
0 & 0 & 0 & 1 \\
1 & 0 & 0 & 0 \\
0 & 1 & 0 & 0
\end{bmatrix} \begin{bmatrix}
0 & -1 & 0 & 0 \\
0 & 1 & 0 & 0 \\
0 & 0 & 0 & -1 \\
0 & 0 & 1 & 0
\end{bmatrix} = \frac{i}{4} \begin{bmatrix}
1 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 \\
0 & 0 & 0 & -1 \\
0 & 0 & 1 & 0
\end{bmatrix}.
\]
Note that \( \hat{I}_x \hat{I}_y \) could also have been calculated as \( \hat{I}_x \hat{I}_y = \hat{I}_x \otimes \hat{I}_y \).

For an \( N \) spin \( I = \frac{1}{2} \) system, there are \( 2^{2N} \) operators that need to be calculated. Again, a similar procedure as described above can be followed. For additional information regarding the derivations of spin operators see reference [19].

### 1.2.1 System Hamiltonians

The spatial and spin elements of the Hamiltonian can be separated into scalar products of tensors in the principal axis system (PAS) [17, 20]. From this point conversion to the irreducible spherical tensor basis allows one to manipulate the system between various coordinate conventions. The principal axes are internal, time independent and move with the molecule. Conversion to an interaction or laboratory reference frame imposes time dependence in the Hamiltonian. From the PAS a set of coordinates can be transformed to an arbitrary axis system via rotation about the Euler angles, denoted here as \( \alpha, \beta, \gamma \). A spherical tensor operator of rank \( v \), denoted \( \mathcal{T}^m_v \) is transformed under rotation into a linear combination of \( 2v + 1 \) operators. Rotation through angle \( \theta \) over an axis, \( a \), is driven by the rotation operator, \( \mathcal{R} \).

\[
\mathcal{T}^m_v, m = [-v, v] \\
\mathcal{R} \mathcal{T}^m_v \mathcal{R}^{-1} = \sum_n \mathcal{D}^v_{nm}(\alpha, \beta, \gamma) \mathcal{T}^n_v
\]  

where \( \mathcal{D}^v_{nm}(\alpha, \beta, \gamma) \) corresponds to the Wigner rotation matrix elements. If a set of spherical tensors are irreducible, commutation of tensor components with angular momentum operators will equivalently define \( \mathcal{T}^m_v \). Equations 1.33 and 1.34 define \( \mathcal{T}^m_v \) in terms of the commutation relationship with \( \hat{I} \).

\[
[I_x \pm iI_y, \mathcal{T}^m_v] = [I_\pm, \mathcal{T}^m_v] = [(v \mp m)(v \pm m + 1)]^{\frac{1}{2}} \mathcal{T}^{(m \pm 1)}_v
\]  

\[
[I_z, \mathcal{T}^m_v] = m \mathcal{T}^m_v
\]
1.2.1.1 Zeeman Interactions

Zeeman terms are invariant under rotation, in as much, the Zeeman Hamiltonian represents interaction between an ensemble of spins and the static magnetic field of the spectrometer, $B_0$.

$$\hat{H}_Z = -\sum_{i}^{\text{spins}} \gamma_i \vec{T}(i) \cdot \vec{B}_0 \quad (1.35)$$

where $B_0$ is the spectrometer field and $\gamma_i$ is the gyromagnetic ratio for spin (i). Setting the z-axis in the direction of the static magnet field and letting $\omega = -\gamma_i |B_0|$, this expression reduces to

$$\hat{H}_Z = \sum_{i}^{\text{spins}} \omega_i \vec{T}_z(i) \quad (1.36)$$

1.2.1.2 Chemical Shift

The chemical shift Hamiltonian corresponds to the energy arising from interactions between the local anisotropic field generated by the motion of the electron cloud surrounding a nuclear spin and the large static magnetic field of the spectrometer [9,17]. Compared to the Zeeman terms, this interaction is energetically “small”. However, the isotropic chemical shift is significant in liquids as it is the part of the Hamiltonian that accounts for the frequency shifts in high resolution experiments. These shifts are usually specific to the individual spins of a given system and the energy of the interaction between the chemical shift and magnetic field scales as strength of the static field. The anisotropic component of the chemical shift Hamiltonian generally has little influence in liquid and gas samples because the terms average out due to fast molecular tumbling. However, the anisotropic terms do influence relaxation. The equation for the magnetic field induced by movement of electrons is given by;

$$\vec{B}_{\text{eff}} = \vec{\omega}_i \cdot \vec{B}_0 \quad (1.37)$$

The term $\vec{\omega}_i$ is the chemical shift or “shielding” tensor and $\vec{B}_{\text{eff}}$ is the effective magnetic field at the ith nucleus. The chemical shift term $\vec{\omega}_i$ is rank two and given
by equation 1.38;

$$\tilde{\varphi} = \begin{bmatrix} \varphi_{xx} & \varphi_{xy} & \varphi_{xz} \\ \varphi_{yx} & \varphi_{yy} & \varphi_{yz} \\ \varphi_{zx} & \varphi_{zy} & \varphi_{zz} \end{bmatrix}$$  \hspace{1cm} (1.38)

The Hamiltonian for the chemical shift interactions over all spins is;

$$\tilde{H}_{cs} = \sum_{i} H_{cs} = \hbar \sum_{i} \gamma_{i} \vec{T}(i) \cdot \tilde{\varphi}(i) \cdot \vec{B}_{0}$$  \hspace{1cm} (1.39)

$$\tilde{H}_{cs}(i) = \hbar \gamma_{i} B_{0} = [I_{x}(i)I_{y}(i)I_{z}(i)] \cdot \begin{bmatrix} \varphi_{xx} & \varphi_{xy} & \varphi_{xz} \\ \varphi_{yx} & \varphi_{yy} & \varphi_{yz} \\ \varphi_{zx} & \varphi_{zy} & \varphi_{zz} \end{bmatrix} \cdot \begin{bmatrix} B_{x} \\ B_{y} \\ B_{z} \end{bmatrix}$$  \hspace{1cm} (1.40)

It is convenient at this point to form a new tensor by taking the dyadic product of \( \vec{T}_{k} \) and \( \vec{B}_{q} \) from equation 1.40, where the \((x, y, z)\) Cartesian axis indices are included by summation over the new indices \( k \) and \( q \). This new tensor, \( \hat{X} \), accounts for the spin field.

$$\tilde{H}_{cs}(i) = \hbar \gamma_{i} B_{0} \sum_{k} \sum_{q} \varphi_{kq}(i) I_{k}(i) B_{q}$$  \hspace{1cm} (1.41)

$$\tilde{H}_{cs}(i) = \hbar \gamma_{i} B_{0} \sum_{k} \sum_{q} \varphi_{kq}(i) X_{kq}(i) = \hbar \gamma_{i} B_{0} [\tilde{\varphi}(i) \otimes \hat{X}(i)]$$  \hspace{1cm} (1.42)

The chemical shift tensor can be broken down into nine components;

$$\tilde{\varphi} = \begin{bmatrix} \varphi_{xx} & \varphi_{xy} & \varphi_{xz} \\ \varphi_{yx} & \varphi_{yy} & \varphi_{yz} \\ \varphi_{zx} & \varphi_{zy} & \varphi_{zz} \end{bmatrix} = \varphi_{iso} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} + \begin{bmatrix} 0 & \lambda_{xy} & \lambda_{xz} \\ \lambda_{yx} & 0 & \lambda_{yz} \\ \lambda_{zx} & \lambda_{zy} & 0 \end{bmatrix} + \begin{bmatrix} \delta_{xx} & \delta_{xy} & \delta_{xz} \\ \delta_{yx} & \delta_{yy} & \delta_{yz} \\ \delta_{zx} & \delta_{zy} & \delta_{zz} \end{bmatrix}$$  \hspace{1cm} (1.43)

In equation 1.43 the components \( \lambda \) and \( \delta \) are used simply to indicate the elements of the chemical shift tensor when represented in the PAS. If it is assumed that \( \tilde{\varphi} \) is symmetrical, then the rank 1 component is zero. When the rank 1 component is non
zero, these terms contribute to chemical shift relaxation without affecting the energy levels in the Hamiltonian [21]. In the PAS $\hat{\varrho}$ reduces to:

$$\hat{\varrho}_{(PAS)} = \begin{bmatrix} \varrho_{xx} & 0 & 0 \\ 0 & \varrho_{yy} & 0 \\ 0 & 0 & \varrho_{zz} \end{bmatrix} = \varrho_{iso} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} + \begin{bmatrix} \delta_{xx} & 0 & 0 \\ 0 & \delta_{yy} & 0 \\ 0 & 0 & \delta_{zz} \end{bmatrix}$$ (1.44)

The chemical shift anisotropy parameter, $\Delta \varrho$ and the assymmetry parameter, $\eta$ are now substituted for anisotropy terms in $\hat{\varrho}_{(PAS)}$ [22].

$$\Delta \varrho = \frac{3}{2} \delta_{zz}$$ (1.45)

and

$$\eta = \frac{(\delta_{xx} - \delta_{yy})}{\delta_{zz}}$$ (1.46)

After some algebra $\hat{\varrho}_{PAS}$ can be written:

$$\hat{\varrho}_{(PAS)} = \varrho_{iso} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} + \delta_{zz} \begin{bmatrix} -\frac{1}{2} (1 - \eta) & 0 & 0 \\ 0 & -\frac{1}{2} (1 + \eta) & 0 \\ 0 & 0 & 1 \end{bmatrix}$$ (1.47)

The elements of $\hat{\varrho}_{(PAS)}$ written as irreducible spherical components are:

$$\varrho_0^0 = -\sqrt{3} \varrho_{iso}$$ (1.48)  
$$\varrho_0^1 = 0$$ (1.50)  
$$\varrho_2^0 = \sqrt{\frac{3}{2}} \delta_{zz}$$ (1.51)  
$$\varrho_2^{\pm 1} = 0$$ (1.52)  
$$\varrho_2^{\pm 2} = \frac{1}{2} \delta_{zz} \eta$$ (1.53)

Conversion of the shift tensor into an arbitrary axis system (AAS) is accomplished through rotation into the PAS for each individual tensor component using equation 1.32. This maneuver results in equation 1.54.

$$\varrho_{v}^{m, AAS} = \sum_{n} D_{m,n}^{\nu} (\alpha, \beta, \gamma) \varrho_{v}^{n, PAS}$$ (1.54)

The chemical shift Hamiltonian can now be defined as,

$$\hat{H}_{cs}(i) = \hbar \gamma_i B_0 \left\{ [\varrho_{0 AAS}^{0}(i)] \hat{X}_{0 AAS}^{0}(i) + \sum_{m=-2}^{2} (-1)^m \varrho_{2}^{-m AAS}^{m}(i) \hat{X}_{2 AAS}^{m}(i) \right\}$$ (1.55)
1.2.1.3 Scalar Coupling

The J-coupling interaction, also called scalar coupling and spin-spin coupling, is the interaction between two spins through bonding electrons within a molecule. The energy of the scalar coupling interaction is given by Equation 1.56.

$$E_j(ij) = \mu_i \cdot \vec{J}'(ij) \cdot \mu_j$$  \hspace{1cm} (1.56)

The scalar coupling tensor, $\vec{J}'$ is related to $\vec{J}$ through the coupling constant. The Hamiltonian for this interaction is given by equation 1.57.

$$\vec{H}_{sc} = \hbar \sum_i \sum_{j > i} \vec{T}(i) \cdot \vec{J}(ij) \cdot \vec{T}(j)$$  \hspace{1cm} (1.57)

Compared with the Zeeman energy, the contribution made by J-coupling is energetically small. The significance of this interaction is the information that it provides in the form of the spin-spin splitting apparent in spectra. The units of $\vec{J}$ are in hertz, coupling constants, henceforth, can be measured in hertz in a high resolution spectrum. Coupling constants for $^{13}$C and $^1$H are typically less than $10^3$ Hz. The scalar coupling tensor can be separated into irreducible Cartesian coordinates in the same way that the chemical shift tensor was broken down in equation 1.43.

$$\vec{J} = \begin{bmatrix} J_{xx} & J_{xy} & J_{xz} \\ J_{yx} & J_{yy} & J_{yz} \\ J_{zx} & J_{zy} & J_{zz} \end{bmatrix} = J_{iso} \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} + \begin{bmatrix} 0 & \lambda_{xy} & \lambda_{xz} \\ -\lambda_{yx} & 0 & \lambda_{yz} \\ -\lambda_{zx} & -\lambda_{zy} & 0 \end{bmatrix} + \begin{bmatrix} \delta_{xx} & \delta_{xy} & \delta_{xz} \\ \delta_{yx} & \delta_{yy} & \delta_{yz} \\ \delta_{zx} & \delta_{zy} & \delta_{zz} \end{bmatrix}$$  \hspace{1cm} (1.58)

Writing equation 1.58 according to the principal axes system produces equation 1.59,

$$\vec{J}_{(PAS)} = J_{iso} + \begin{bmatrix} \delta_{xx} & 0 & 0 \\ 0 & \delta_{yy} & 0 \\ 0 & 0 & \delta_{zz} \end{bmatrix}$$  \hspace{1cm} (1.59)

The irreducible spherical tensor components for $\vec{J}$ in the PAS are then;

$$J_0^0 = -\sqrt{\frac{1}{3}} \text{Tr}\{\vec{J}\}$$  \hspace{1cm} (1.60)

$$J_0^1 = 0$$  \hspace{1cm} (1.61)
\[ J_1^\pm = 0 \]  
(1.62)  
\[ J_2^0 = \frac{\sqrt{3}}{2}\delta_{zz} \]  
(1.63)  
\[ J_2^\pm = 0 \]  
(1.64)  
\[ J_2^2 = \frac{1}{2}(\delta_{xx} - \delta_{yy}) \]  
(1.65)

The expression for scalar coupling in PAS can now be rotated into an arbitrary axis system;

\[ J_{m}^{v}_{\text{AAS}} = \sum_{n} D_{m,n}^{v}(\alpha, \beta, \gamma) J_{m}^{v}_{\text{PAS}} \]  
(1.66)

For a symmetric \( \hat{J} \), the scalar coupling Hamiltonian has both non zero isotropic and anisotropic terms which, according to equation 1.59, are tensors of rank 0 and rank 2. The scalar component is invariant under rotation and contributes to the static Hamiltonian of the total spin system while the anisotropic components contribute to relaxation. The scalar coupling Hamiltonian in AAS is given by equation 1.67.

\[ \hat{H}_{sc}(ij) = \hbar \left\{ [\hat{J}_{0}^{0}_{\text{AAS}}(ij)]^{-1} + \sum_{m=-2}^{2} (-1)^{m} \hat{J}_{2}^{-m}_{\text{AAS}}(ij)] \right\} \]  
(1.67)

### 1.2.1.4 Dipolar Coupling

The energy and Hamiltonian describing the interaction between two dipoles in a quantum system separated by \( \vec{r} \) are described by equations 1.68 and 1.69, where \( \mu = \gamma \hbar \vec{T} \).

\[ \hat{E}_{\text{dip}} = \sum_{i} \sum_{j>i}^{\text{spins}} \sum_{k} \sum_{l} \left[ \frac{\vec{\mu}_i \cdot \vec{\mu}_j}{r_{ij}^3} - 3 \frac{(\vec{\mu}_i \cdot \vec{\tau}_{ij})(\vec{\mu}_j \cdot \vec{\tau}_{ij})}{r_{ij}^5} \right] \]  
(1.68)

\[ \hat{H}_{\text{dip}} = \sum_{i} \sum_{j} \frac{\gamma_i \gamma_j \hbar^2}{r_{ij}^3} \left[ \hat{T}(i) \cdot \hat{T}_j - 3 \frac{[\hat{T}(i) \cdot \vec{\tau}_{ij}][\hat{T}(j) \cdot \vec{\tau}_{ij}]}{r_{ij}^5} \right] \]  
(1.69)

The Hamiltonian can be separated into spatial and spin components;

\[ \hat{H}_{\text{dip}}(i) = \frac{\hbar^2 \gamma_i \gamma_j}{r_{ij}^3} = [I_x(i)I_y(i)I_z(i)] \cdot \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \ D_{yx} & D_{yy} & D_{yz} \ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}_{ij} \cdot \begin{bmatrix} I_x(j) \ I_y(j) \ I_z(j) \end{bmatrix} \]  
(1.70)
where $\hat{D}$ is the dipolar tensor. The terms in $I$ for spins $i$ and $j$ are contained in the new tensor, $\hat{X}$. The principal axis for the dipolar tensor is such that the vector between spins $i$ and $j$, $\vec{r}_{ij}$, is aligned with the $z$ axis in a Cartesian coordinate system. In the PAS, $\hat{D}(ij)$ reduces to its rank 2 component.

$$\hat{D}_{(PAS)} = \begin{bmatrix} 2 & 0 & 0 \\ 0 & -1 & 0 \\ 0 & 0 & -1 \end{bmatrix}_{ij} \quad (1.71)$$

For $\hat{D}_{PAS}(ij)$, there is one non-zero expression when written in the spherical tensor basis;

$$\hat{D}^0_2 = -\sqrt{6} \quad (1.72)$$

$$D^m_{\alpha\beta\gamma\delta} = \sum_n D^\nu_{m,n} (\alpha, \beta, \gamma) D^n_{\nu,PAS} \quad (1.73)$$

Using equation 1.73 the dipolar Hamiltonian for an arbitrary axis system can be written:

$$\hat{H}_d = \sum_{i} \sum_{j} \frac{\gamma_{ij}}{r^3_{ij}} \frac{2}{\Delta m} (-1)^m D^m_{\alpha\beta\gamma\delta} X^m_{\alpha\beta\gamma\delta} \quad (1.74)$$

### 1.3 Average Hamiltonian Theory

The Louville-von Neumann equation describes the changes occurring in a spin system over the course of an NMR experiment. The NMR sample is considered a closed system with finite dimension that undergoes unitary evolution in Hilbert space. The dynamics of the system are described by the density operator, which itself obeys the conditions directed by the von Neumann equation [23]. Beginning with the Schrödinger equation, the time evolution of the density operator is written

$$\rho(t) = \sum_{\alpha=1}^{Z} \langle \Psi^{\alpha}(t) | \Psi^{\alpha}(t) \rangle \quad (1.75)$$
Taking the derivative with respect to time yields equation 1.76, which is the quantum form of Liouville’s theorem, the Liouville - von Neumann equation.

\[ \frac{\partial \rho}{\partial t} = \frac{1}{i\hbar} [\hat{H}, \rho] \]  
(1.76)

The formal solution to equation 1.76 is

\[ \rho(t) = U(t)\rho(0)U^{-1}(t) \]  
(1.77)

Where \( U \) is the propagator for the system and \( U(t, t_0) \) adheres to the Schrödinger type equation of motion;

\[ \frac{d(U)(t, t_0)}{d(t)} = -i[H(t), U(t)] \]  
(1.78)

Changes in the density matrix for discrete time intervals over the course of an NMR experiment are driven by successive propagators which correspond to these time intervals [24]. The integral form of equation 1.78 is

\[ U(t, t_0) = T \exp \left\{ -i \int_{t_0}^{t} dt H(t) U(t, t_0) \right\} \]  
(1.79)

where \( T \) is the Dyson time ordering operator. The form of the propagator depends upon the characteristics of the Hamiltonian [24–26]. When \( H \) is time independent, integrating equation 1.79 yields

\[ U(t, t_0) = \exp \{ -iH\tau \} \]  
(1.80)

where \( \tau = t - t_0 \). If the Hamiltonian commutes at all points across \([t_0, t]\), such that \([H(t'), H(t'')] = 0\) for all \([t'_0, t'_0]\), the propagator is

\[ U(t, t_0) = \exp \left\{ -i \int_{t_0}^{t} dt' H(t') \right\} \]  
(1.81)

When \([H(t), H(t')] \neq 0\) for \( t \neq t' \) the propagator cannot be derived analytically. In this scenario it is possible to use average Hamiltonian theory to define an effective time independent Hamiltonian [27]. Equation 1.79 becomes

\[ \exp \{-i\bar{H}\tau \} \equiv T \exp \left\{ -i \int_{t_0}^{t} dt H(t) U(t, t_0) \right\} \]  
(1.82)
The effective Hamiltonian can be expanded to the $n$th order via the Magnus expansion [28, 29].

\[ \mathcal{H} = \mathcal{H}^{(1)} + \mathcal{H}^{(2)} + \mathcal{H}^{(3)} + \ldots \tag{1.83} \]

\[ \mathcal{H} = \sum_{n=0}^{\infty} \mathcal{H}^{(n)} \tag{1.84} \]

\[ \mathcal{H}^{(1)} = \frac{1}{\tau} \int_{t_0}^{t} dt' H(t') \tag{1.85} \]

\[ \mathcal{H}^{(2)} = \frac{1}{2i\tau} \int_{t_0}^{t} dt' \int_{t_0}^{t'} dt'' [H(t'), H(t'')] \tag{1.86} \]

\[ \mathcal{H}^{(3)} = -\frac{1}{6\tau} \int_{t_0}^{t} dt' H(t') \int_{t_0}^{t'} dt'' \int_{t_0}^{t''} dt''' [H(t'), [H(t''), H(t''')]] + [[H(t'), H(t'')], H(t''')] \tag{1.87} \]

The Magnus expansion is Hermitian in all orders of $n$, resulting in a Hermitian effective Hamiltonian for any order of truncation, henceforth insuring that the propagator is unitary [24].

### 1.3.1 The Interaction Frame

Transforming into an interaction representation may prove beneficial in the case where the Hamiltonian can be expressed as a sum of its parts. Separating terms of the Hamiltonian according to their “size” increases the likelihood that the convergence condition, $||H(t)||\tau \ll 1$ for $t'_0$, will be met for increasing orders of the Magnus expansion. Consider the Hamiltonian represented in equation 1.88, where $H(t)$ represents the total system Hamiltonian, $H_B$ is the “big” term and $H_S$ is the “small” term.

\[ H(t) = H_B(t) + H_S(t) \tag{1.88} \]

The term $H_B(t)$ is chosen so that the propagator may be expressed analytically;

\[ \frac{d}{dt} U_B(t, t_0) = -iH_B(t)U_B(t, t_0) \tag{1.89} \]

\[ U_B(t_0, t_0) = 1 \tag{1.90} \]
The interaction frame propagator, \( U(t, t_0) \), is defined as;

\[
U(t, t_0) = U_B(t, t_0)U(t, t_0) \tag{1.91}
\]

The interaction frame Hamiltonian, \( \mathcal{H}(t) \), can now be defined with respect to \( U(t, t_0) \).

\[
\frac{d}{dt}U(t, t_0) = -i \left[ U_B^\dagger(t, t_0)H(t)U_B(t, t_0) - iU_B^\dagger(t, t_0)\left( \frac{d}{dt}U_B(t, t_0) \right) \right] U(t, t_0) \tag{1.92}
\]

\[
\mathcal{H} = U_B^\dagger(t, t_0)H(t)U_B(t, t_0) - iU_B^\dagger(t, t_0)\left( \frac{d}{dt}U_B(t, t_0) \right) \tag{1.93}
\]

\[
\mathcal{H}(t) = \mathcal{H}_S(t) = U_B^\dagger(t, t_0)H_S(t)U_B(t, t_0) \tag{1.94}
\]

The Interaction frame Hamiltonian derived above can now be used to construct and average Hamiltonian.

### 1.4 Pathway Selective Pulses

The purpose of designing a pathway selection scheme is to gain greater control over the direction that a quantum system takes through evolution. The practice of pathway selection is used in optical spectroscopy as well as in NMR. In both cases the “selection” is generally made by combining a series of experiments such that the signal produced is representative of a select set of all evolution pathways available from the multiple experiments. Phase cycling, for example, is a common type of pathway selection used in NMR to filter select signals arising from specific coherence pathways.

Walls’s pathway selective pulse (PSP) method converts a pathway selection scheme into a coherent pulse in which a single experiment can be applied to evaluate the availability of pathways in a system [6]. Suppose there exists a closed, n-dimensional quantum system defined by the density matrix \( (\frac{1}{n})\mathbb{1} + \hat{\rho}(t) \), where \( \mathcal{L} \) defines a subset of operators of dimension M, \( \mathcal{L} = \{ \hat{O}_1, \hat{O}_2, ..., \hat{O}_M \} \), \( \mathbb{1} \) is the identity matrix and \( \text{Tr}[\hat{\rho}(t)] = 0 \). Expanding \( \hat{\rho} \) into an M dimensional set of operators such that \( \hat{\rho}(t) = \sum_{k=1}^{M} k(t)\hat{O}_k \) for all \( t \) and assuming that \( \hat{\rho}(t_0) = \hat{O}_j \), then evolution under the
The Hamiltonian, $\hat{H}_\alpha$, transforms $\hat{\rho}(t_0)$ to $\hat{\rho}(t_N)$ where,

$$\hat{\rho}(t_N) = \hat{U}_\alpha(t_N, t_0)\hat{\rho}(t_0)\hat{U}_{\alpha}^\dagger(t_N, t_0) = \sum_{k=1}^{M}(t_N, t_0)\hat{O}_k$$  \hspace{1cm} (1.95)

The propagator under $\hat{H}_\alpha$ in equation 1.95 is given by equation 1.96 where $\hat{T}$ is the Dyson time ordering operator.

$$\hat{U}_\alpha(t_N, t_0) = \hat{T}\exp\left[-\frac{i}{\hbar}\int_{t_0}^{t_N} dt'\hat{H}_\alpha(t')\right]$$  \hspace{1cm} (1.96)

The term, $c_{kj}^\alpha(t_N, t_0)$, represents the transition amplitude when evolving from $\hat{\rho}(t_0) = \hat{O}_j$ to $\hat{O}_j$ under the propagator, $\hat{U}_\alpha(t_N, t_0)$

$$c_{kj}^\alpha(t_N, t_0) = \left\{\frac{\text{Tr}[\hat{O}_k^\dagger\hat{U}_\alpha(t_N, t_0)\hat{O}_j\hat{U}_{\alpha}^\dagger(t_N, t_0)]}{\text{Tr}[\hat{O}_k^\dagger\hat{O}_k]}\right\}$$  \hspace{1cm} (1.97)

Suppose the propagator can be separated into the product of $N$ time ordered propagators such that $\hat{U}_\alpha(t_N, t_0) = \hat{T}\Pi_{k=0}^{N-1}\hat{U}_\alpha(t_{k+1}, t_k)$. The evolution of the system can be described as $M^N$ different $N$-step evolution pathways where the density matrix is represented as $\hat{\rho} = \hat{O}_j \longrightarrow \hat{\rho}(t_N)$ for the basis $\mathcal{L}$. Using a pathway selection scheme it is possible to choose a subset of the $M^N$ evolution pathways by combining results of multiple experiments, $N_{\text{exp}} \leq M^N$. The deviation density matrix and propagator are given by;

$$\bar{\rho} = \sum_{k=1}^{N_{\text{exp}}} \lambda_k\hat{\rho}_k(t_N)$$  \hspace{1cm} (1.98)

$$\hat{\rho}_k(t_N) = \hat{U}_k(t_N, t_0)$$  \hspace{1cm} (1.99)

where $\lambda_k$ is the weighting factor for experiment “$k$”.

A PSP may be generated by converting any PSS, however, the PSS must use only real $\lambda_k$ in order to insure that $\bar{\rho}$ is Hermetian. Because $\bar{\rho}$ is Hermetian, a pathway and its corresponding conjugate pathway must both contribute to $\bar{\rho}$.

The general method for designing a PSP from a PSS begins by assuming that a time dependent Hamiltonian can be generated such that

$$\frac{\hat{H}_0}{\hbar} = \eta\hat{\rho}(t_0)$$  \hspace{1cm} (1.100)
where $\eta$ is the proportionality constant. The propagator under $\hat{H}_0$ for time $t_k = \lambda_k \tau$ is defined by

$$\hat{P}_k = \exp \left[ - \left( \frac{it_k}{\hat{H}_0} \right) \right] = \exp[-i\tau \lambda_k \eta \hat{\rho}(t_0)] \tag{1.101}$$

If the time reversed propagator for $k = 1$ to $k = N_{eq}$, $\hat{U}_k^\dagger(t_N, t_0)$, can be generated by experiment, then the propagator for pulse block $\hat{U}_k(t_N, t_0) = \hat{P}_k - \hat{U}_k(t_N, t_0)$, is the equivalent to evolving under a Hamiltonian that is proportional to the deviation density matrix of the $k$th experiment. This condition is illustrated by equation 1.102.

$$\hat{U}_k(t_N, t_0) \hat{P}_k \hat{U}_k^\dagger(t_N, t_0) = \exp \left[ -i\eta \tau \lambda_k \hat{U}_k(t_N, t_0) \hat{P}_k \hat{U}_k^\dagger(t_N, t_0) \right] = \exp[-i\eta \tau \lambda_k \hat{\rho}_k(t_N)] \tag{1.102}$$

The PSP is generated by concatenating different pulse blocks for various $N_{exp}$ and deriving the overall propagator, $\hat{U}_{1,2,3,...N}$, where the subscript denotes the order of the pulse block.

$$\hat{U}_{1,2,3,...N} = \hat{T} \prod_{k=1}^{N_{exp}} \hat{U}_k(t_N, t_0) \hat{P}_k \hat{U}_k^\dagger(t_N, t_0) = \hat{T} \prod_{k=1}^{N_{exp}} \exp[-i\eta \tau \lambda_k \hat{\rho}_k(t_N)] \tag{1.103}$$

Average Hamiltonian theory is now used to rewrite the propagator as $\hat{U}_{1,2,3,...N_{exp}} \equiv \exp(-i\tau \bar{H}_{avg})$. The average Hamiltonian is defined by $\bar{H}_{avg} = \sum_{j=1}^{\infty} \bar{H}^{(j)}_{avg}$. The system evolves for time $\tau$ under $\bar{H}_{avg}$ for $j$ contributions from all $\bar{H}^{(j)}_{avg}$. For the condition $||\tau \lambda_k \eta \hat{\rho}(t_0)|| \ll \frac{\tau \bar{\eta}}{2}$ and $N_{exp}||\eta \bar{\rho}|| \leq 2\pi$, the average overall Hamiltonian, $\bar{H}_{avg}$ can be approximated;

$$\bar{H} \approx \bar{H}_{avg}^{(1)} = \frac{1}{\tau} \sum_{k=1}^{N_{exp}} \tau \lambda_k \eta \hat{\rho}_k(t_N) = \eta \bar{\rho} \tag{1.104}$$

For the conditions of equation 1.104, $\hat{U}_{1,2,3,...N_{exp}} \approx \exp(-i\tau \eta \bar{\rho})$. The order of the pulse blocks do not affect $\bar{H}_{avg}^{(1)}$ in 1.104, however, it does affect higher orders of $\bar{H}_{avg}^{(j)}$.

In the next chapter a PSP referred to as the Reverse Inept Pathway Selective Pulse (RIPSP) is presented that is based on the evolution pathways under the reverse INEPT [30] sequence. The RIPSP conditionally excites only $^1\text{H}$ spins that are coupled to a $^{13}\text{C}$ spins in $I_n S$ spin systems, producing “pure” $I$ spin rotations by an angle that depends on the heteronuclear coupling constant, $J_{IS}$. Additionally, the RIPSP
is shown to sustain coherence transfer between $^1$H spins that are not directly coupled to a $^{13}$C spins via $^1$H – $^1$H spin-spin coupling in particular systems.
CHAPTER 2

Conditional Rotations of Heteronuclear Coupled Spins

The pathway selection scheme presented in 2 was used to develop a pathway selective pulse (PSP) based on the evolution pathways under the reverse INEPT [30] sequence. This pulse, referred to as the Reverse Inept Pathway Selective Pulse (RIPSP), conditionally excites only those $^1$H spins that are coupled to a $^{13}$C spin. In this chapter, the theory behind the RIPSP applied to $I_nS$ spin systems is presented, where it is shown that the RIPSP can generate “pure $I$ spin rotations” by an angle that depends on the heteronuclear coupling constant, $J_{IS}$. The $^1$H-$^1$H spin-spin coupling during the RIPSP is shown to generate coherence transfers to other $^1$H spins that are not directly coupled to a $^{13}$C spin. Experimental demonstrations of the nutation curves under the RIPSP sequence in $^{13}$C-labeled chloroform ($IS$), dichloromethane ($I_2S$) and toluene ($I_3S$) samples are presented to evaluate the rotational properties of the RIPSP propagator, $\hat{U}_{RIPSP}$. Finally, experimental results using unlabeled 2,3-dibromopropionic acid and brucine samples demonstrate that the RIPSP can selectively excite $^1$H spins coupled directly and indirectly to $^{13}$C spins [31].

2.1 Background

Selective excitation is an important component in the construction of NMR experiments. Most types of selective excitation fall into one of two categories; frequency selection and coherence selection. An example of a frequency selective pulse which
has been applied to observe $^{13}$C-coupled $^1$H spins is low-amplitude frequency selective pulses at $\nu_0 \pm \frac{J_{1S}}{2}$ (where $J_{1S}$ is the heteronuclear coupling constant (in Hz) and $\nu_0$ is the nominal resonance of the $^1$H spin in the absence of heteronuclear coupling) [32]. However, any $^1$H resonance with a frequency near $\nu_0 \pm \frac{J_{1S}}{2}$, even those not coupled to a $^{13}$C spin, will also be excited. This is due to the fact that frequency-selective pulses excite spins based solely on transition frequency and not on the origin of the transition frequency. This transition occurs between two eigenstates of the system’s Hamiltonian $\hat{H}$, $|j\rangle$ and $|k\rangle$ and depends upon the transition frequency between the two states, $
u_{jk} = \frac{E_j - E_k}{h}$, where $E_j$ and $E_k$ are the energies of the states $|j\rangle$ and $|k\rangle$, respectively, and $h$ is Planck’s constant [33, 34]. In order to avoid exciting $^1$H spins that are not coupled to a $^{13}$C but resonate near the $^{13}$C-satellites, selective excitation based upon the presence of a heteronuclear spin-spin interaction in $\hat{H}$ has been developed. For example, $^1$H spins experience a $\Theta_{\text{rotation}} = \pi$ or $\Theta_{\text{rotation}} = \frac{\pi}{2}$ bilinear rotation in the BIRD [35] and TANGO [36] sequences, respectively, only in the presence of a nonzero coupling to a $^{13}$C spin. Sørensen generalized these types of bilinear excitation sequences with the BANGO [37] and BIG-BIRD [38], [39] sequence that can be used to perform arbitrary rotations of the $^{13}$C-satellites. For these kinds of bilinear selective pulses, the timing of the $^1$H and $^{13}$C RF pulses depend upon $J_{1S}$. For molecules with a distribution of heteronuclear coupling constants the so-called “J-mismatch” can occur. Exciting transitions based on the internal structure and/or rotational properties of $\hat{H}$ have also been developed. For example, filtering signals based on the types of multiple-quantum (MQ) coherences that can be generated during the course of an experiment is routinely employed to selectively detect spins depending on differences in the internal structure of $\hat{H}$. An HMQC experiment [40], for example, can be used to detect the signal from spin systems with a nonzero heteronuclear spin-spin interaction. Besides being used for selective filtering, differences in the internal structure of $\hat{H}$ can also be used to selectively excite certain types of coherences. For example, if $\hat{H}$ contains spin-spin couplings, certain MQ coherences can be selectively excited by a series of radiofrequency (RF) pulses
that generate a particular MQ Hamiltonian. This excitation depends either on the rotational properties of the spin Hamiltonian, as used, for example, in the selective pumping of MQ-coherences [41, 42], or on the rotational properties of both the spin and spatial tensors in $\hat{H}$ such as under magic-angle spinning, for example [43, 44].

### 2.2 Theory

In this section, a theoretical description of the RIPSP sequence shown in Figure 2.1 is discussed, followed by an analysis of the effects of $^1\text{H}^-^1\text{H}$ spin-spin coupling during the RIPSP sequence.

#### 2.2.1 Theoretical Description of the RIPSP Sequence Applied to $I_nS$ Spin Systems

The reverse INEPT PSP or RIPSP sequence shown in Figure 2.1 generates a selective linear rotation of $I$ spins in an $I_nS$ spin system. To understand the various spin transformations that occur during the RIPSP sequence, consider the propagator for the pulse block in Figure 2.1. $\hat{U}_{IS,\pm}$ is given by,

\[
\hat{U}_{IS,\pm} = \hat{P}_I^I\left(\frac{\pi}{2}\right)\hat{P}_S^S\left(\frac{\pi}{2}\right)\hat{U}_+\hat{U}_+\hat{P}_I^I\left(\pi\right)\hat{U}_+\hat{U}_+\hat{P}_S^S\left(\frac{\pi}{2}\right)\hat{P}_-^S\left(\frac{\pi}{2}\right) \tag{2.1}
\]

Here, $\hat{P}_I^I(S)(\theta)$ represents a rotation about a transverse axis of phase $\phi$ where the flip-angle $\theta$ is applied to the $I(S)$ spins and

\[
\hat{U}_+ = e^{-\frac{i\theta}{\hbar}\hat{H}}\hat{P}_I^I(\pi)\hat{P}_S^S(\pi) e^{-\frac{i\theta}{\hbar}\hat{H}}\hat{P}_S^S(\pi - \theta) e^{-\frac{i\theta}{\hbar}\hat{H}}\hat{P}_I^I(\pi)\hat{P}_S^S(\pi) e^{-\frac{i\theta}{\hbar}\hat{H}} \tag{2.2}
\]

where the $\pm$ subscript in Equation 2.2 indicates the phase of the imperfect $\pi$-pulses applied to the $S$ spin, $\pm X$, and $\hat{H}$ is the Hamiltonian in the absence of RF irradiation. Unless explicitly stated, the phases of the $I$ spin $\pi-$pulses in Equations 2.1 and 2.2 are chosen to be either $\pm X$. 
Figure 2.1: Reverse INEPT PSP (RIPSP) based upon the evolution pathway selected in the reverse INEPT sequence [30], \( \hat{S}_I \rightarrow \hat{I}_I \hat{S}_S \rightarrow \hat{I}_I \hat{S}_I \rightarrow \hat{I}_I \). An optional z-filter [45] is placed at the end of the RIPSP sequence and before acquisition in order to remove antiphase \( I \) spin magnetization generated by \( ^1H-^1H \) spin-spin couplings during the RIPSP. For \( 2\pi J_{IS} \tau_1 \ll 1 \) and \( 2\pi J_{IS} \tau_2 \ll 1 \), the propagator for the RIPSP is \( \hat{U}_{RIPSP} \approx P_{\pm X} (\Theta_{RIPSP}) \), which represents an \( I \) spin rotation about the \( \pm \hat{x} \) axis by an angle \( \Theta_{RIPSP} = 64\theta^2 J_{IS}^2 \tau_1 \tau_2 \). Subtracting the \( ^1H \) signal under \( \hat{U}_{RIPSP,+} \) from the \( ^1H \) signal under \( \hat{U}_{RIPSP,-} \) significantly suppresses the \( ^1H \) signal from non \( S \)-spin containing molecules. Note that the phase of the \( \frac{\pi}{2} \) pulses in the z-filter are \( \pm X \) in order to provide the maximum \( ^1H \) signal.
The IS spin system $\hat{U}_{\pm}$ in Equation 2.2 can be rewritten as:

$$
\hat{U}_{\pm} = \hat{P}_{X}^{S}(\pi)e^{i4\pi J_{IS}T_{1}\hat{I}_{Z}\hat{S}_{Z}}\hat{P}_{X}^{S}(-\theta)e^{-i4\pi J_{IS}T_{1}\hat{I}_{Z}\hat{S}_{Z}}
$$

$$
= \hat{P}_{X}^{S}(\pi)e^{\pm i\theta}[\hat{S}_{X}\cos(2\pi J_{IS}T_{1})-2\hat{I}_{Z}\hat{S}_{Y}\sin(2\pi J_{IS}T_{1})]
$$

The propagator for $\hat{U}_{\mp}\hat{U}_{\pm}\hat{P}_{I}(\pi)\hat{U}_{\pm}\hat{U}_{\mp}$ is determined by Equation 2.3 such that,

$$
\hat{U}_{\mp}\hat{U}_{\pm}\hat{P}_{I}(\pi)\hat{U}_{\pm}\hat{U}_{\mp} = \hat{P}_{I}(\pi)e^{\mp i\theta}[\hat{S}_{X}\cos(2\pi J_{IS}T_{1})-2\hat{I}_{Z}\hat{S}_{Y}\sin(2\pi J_{IS}T_{1})]
$$

$$
\times e^{\pm i\theta}[\hat{S}_{X}\cos(2\pi J_{IS}T_{1})+2\hat{I}_{Z}\hat{S}_{Y}\sin(2\pi J_{IS}T_{1})]
$$

$$
\times e^{\mp i\theta}[\hat{S}_{X}\cos(2\pi J_{IS}T_{1})-2\hat{I}_{Z}\hat{S}_{Y}\sin(2\pi J_{IS}T_{1})]
$$

$$
\approx \hat{P}_{I}(\pi)e^{\pm 180^\circ \sin(2\pi J_{IS}T_{1})\hat{I}_{Z}\hat{S}_{Y}+O[\theta^3]}
$$

Average Hamiltonian theory (AHT) [27] was used to approximate the last line in Equation 2.3 by adding the exponents of the individual propagators. Because of the symmetry of the propagator in Equation 2.3, the second-order average Hamiltonian is the next nonzero term [21], which scales as $O[\theta^3]$. Using Equation 2.3, $\hat{U}_{IS,\pm}$ in Equation 2.1 can be rewritten as:

$$
\hat{U}_{IS,\pm} = \hat{P}_{I}(\pi)e^{8\theta \sin(2\pi J_{IS}T_{1})\hat{I}_{Z}\hat{S}_{Z}} \tag{2.3}
$$

Where the imperfection to the $S$ spin $\pi$-pulses, $\theta\hat{S}_{\pm}$, has been transformed into an effective Hamiltonian proportional to $\theta\hat{I}_{Z}\hat{S}_{Z}$. Transformations $\theta\hat{S}_{\pm} \rightarrow \theta\hat{I}_{Z}\hat{S}_{\pm} \rightarrow \theta\hat{I}_{Z}\hat{S}_{Z}$ have been performed for the effective Hamiltonian of the propagator $\hat{U}_{IS,\pm}$. Converting the effective Hamiltonian for the $\hat{U}_{IS,\pm}$ pulse block into $\hat{I}_{\pm}$ generates a rotation of the $I$ spins caused by interleaving the $\hat{U}_{IS,\pm}$ propagator in Equation 2.1 between periods of evolution under the heteronuclear interaction shown in Figure 2.1. The propagator for one loop ($n_{l} = 1$) of the RIPSP sequence, $\hat{U}_{RIPSP,\pm}$, is then given
by;

$$\hat{U}_{RIPSP,\pm} = e^{\pm i 4\theta \sin(2\pi J_{IS}\tau_1)[2\hat{I}_Y \hat{S}_Z \cos(2\pi J_{IS}\tau_2) - \hat{I}_X \sin(2\pi J_{IS}\tau_2)]} \times e^{\mp i 8\theta \sin(2\pi J_{IS}\tau_1)[2\hat{I}_Y \hat{S}_Z \cos(2\pi J_{IS}\tau_2) + \hat{I}_X \sin(2\pi J_{IS}\tau_2)]} \times e^{\pm i 4\theta \sin(2\pi J_{IS}\tau_1)[2\hat{I}_Y \hat{S}_Z \cos(2\pi J_{IS}\tau_2) - \hat{I}_X \sin(2\pi J_{IS}\tau_2)]} \approx e^{\mp 16i\theta \sin(2\pi J_{IS}\tau_2) \sin(2\pi J_{IS}\tau_1) \hat{I}_X + \mathcal{O}[\theta^3]} = \hat{P}^I_{\pm X}(\Theta_1)$$

where $\Theta_1 = 16\theta \sin(2\pi J_{IS}\tau_2) \sin(2\pi J_{IS}\tau_1)$ is the effective angle of rotation under the RIPSP sequence for an IS spin system. AHT was used again to combine the exponents of the individual propagators in Equation 2.4. Due to symmetry, the next higher-order correction is again of order $\mathcal{O}[\theta^3]$. From Equation 2.4, it is apparent that $\hat{U}_{RIPSP,\pm}$ is equivalent to a pure spin rotation about the $\pm X$ axis of angle $\Theta_1$ for those $I$ spins with $J_{IS} \neq 0$. When $J_{IS} = 0$, $\hat{U}_{RIPSP,\pm} \approx \hat{I}$, no $I$ spin rotation is generated. However, an $I$ spin rotation is always generated for $J_{IS} \neq 0$ and the amount of excitation depends on $J_{IS}$. This can be seen in Figure 2.2 where the $^{13}$C-edited $^1$H spectra under the RIPSP with z-filter is displayed for DBPA and brucine.

Assignment of the individual protons for the 90-acquire and RISPSP experiments are provided in Table 2.1. Because of the short acquisition time for brucine, the signals do not represent quantitative data; the signals observed under the RIPSP were corrected using a saturation correction factor calculated by taking the ratio of expected to experimentally determined integrals. Spectra for DBPA and brucine obtained from the RIPSP with z-filter are shown in Figure 2.2.

For an $I_2 S$ spin system, calculations similar to those in Equations [2.1 - 2.3] leads to a propagator of the same form as $\hat{U}_{RIPSP,\pm}$ in Equation 2.4:

$$\hat{U}_{RIPSP,\pm} = \hat{P}^I_{\pm X}(\Theta_2) \text{ where } \Theta_2 = 4\theta \sin(4\pi J_{IS}\tau_2) \sin(4\pi J_{IS}\tau_1)$$
Figure 2.2: The $^{13}$C-edited $^1$H spectra under the RIPSP with z-filter sequence are shown for DBPA (A) and brucine (B). Integrals for the $^{13}$C-satellites are provided in Tab. 2.1. For DBPA (A), the integrals were quantitative in an approximate 1:1:1 ratio. This is due to the small chemical ranges for $^1$H and $^{13}$C as well as the observed $^1J_{CH}$ for the $^{13}$C isotopomers being the nearly identical. For brucine (B), minimal excitation for $^{13}$C-satellites for the $^1$H was observed as shown in Tab. 2.1.
<table>
<thead>
<tr>
<th>Brucine</th>
<th>Relative Integrals from a 90-acquire exp.</th>
<th>Expected Relative Integrals</th>
<th>Saturation Correction factor</th>
<th>Relative Integral from RIPSP &amp; z-filter exp.</th>
<th>Corrected Relative Integral</th>
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<td>1</td>
<td>1</td>
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<td>1</td>
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<td>20β/11β</td>
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<td>0.8230</td>
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<td>18β</td>
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<td>1.3617</td>
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</tr>
<tr>
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<td>11α</td>
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<td>Expected Relative Integrals</td>
<td>Saturation Correction factor</td>
<td>Relative Integral from RIPSP &amp; z-filter exp.</td>
<td>Corrected Relative Integral</td>
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Table 2.1: Relative integrals under both the 90-acquire and RIPSP with z-filter for brucine and dibromopropionic acid. Experimentally determined assignments as given in Fig. 2.2. Saturation correction factors were calculated by taking the ratio of the expected to the observed integrals from the 90-acquire.
For an $I_3S$ spin system;

$$
\hat{U}_{\text{RIPSP}, \pm} = \exp \left( \mp i \left[ \Theta_3 \hat{I}_X + 8\theta \sin^3(2\pi J_{IS}\tau_2) \sin^3(2\pi J_{IS}\tau_1) \left( \hat{I}_{X1}\hat{I}_{X2}\hat{I}_{X3} \right) + 8\theta \sin(2\pi J_{IS}\tau_2) \cos^2(2\pi J_{IS}\tau_2) \sin^3(2\pi J_{IS}\tau_1) \times \right.ight.

\left. \left. (\hat{I}_{X1}\hat{I}_{Y2}\hat{I}_{Y3} + \hat{I}_{X2}\hat{I}_{Y1}\hat{I}_{Y3} + \hat{I}_{X3}\hat{I}_{Y1}\hat{I}_{Y2}) \right] \right)
$$

\begin{equation}
\text{(2.4)}
\end{equation}

where $\Theta_3 = 16\theta \sin(2\pi \tau_1) \cos^2(2\pi \tau_1) \sin(2\pi \tau_2) \cos^2(2\pi \tau_2)$. In this case, the effective Hamiltonian for the $\hat{U}_{\text{RIPSP}, \pm}$ propagator in Equation 2.4 contains a pure rotation term, $\Theta_3 \hat{I}_X$, and also multispin single- and triple-quantum terms. The reverse INEPT “pathway” used to design the RIPSP [6] is responsible for generating these multispin terms in addition to the rotation terms. When $2\pi J_{IS}\tau_1 \ll 1$ and $2\pi J_{IS}\tau_2 \ll 1$, the RIPSP will generate identical rotations in $IS$, $I_2S$, and $I_3S$ spin systems of angle $\Theta_1 \approx \Theta_2 \approx \Theta_3 \approx \Theta_{\text{RIPSP}} = 64\theta \pi^2 J_{IS}^2 \tau_1\tau_2$ and when $J_{IS} = 0$ then $\Theta_{\text{RIPSP}} = 0$. The choice of delays in the RIPSP sequence can, in principle, be arbitrary so long as $2\pi J_{IS}\tau_1 \ll 1$ and $2\pi J_{IS}\tau_2 \ll 1$. However, in order to achieve a desired overall rotation of the $I$ spins in the shortest amount of time, the choice of $\tau_1$ and $\tau_2$ are partly determined by $J_{IS}$. The overall rotation under $n_l$ repetitions of the RIPSP, $n_l\Theta_{\text{RIPSP}}$, thus depend on the heteronuclear coupling constant $J_{IS}$. If $2\pi J_{IS}\tau_1 \ll 1$ and $2\pi J_{IS}\tau_2 \ll 1$, then a pure rotation of the $I$ spins is always generated using the RIPSP sequence, independent of the actual values for the delays $\tau_1$ and $\tau_2$. When evolution during the applied pulses (i.e., taking the $\delta$—pulse limit) is neglected, the method of Lagrange multipliers can be used to minimize the RIPSP cycle time, $\tau_c = 64\tau_1 + 12\tau_2$, subject to the constraint that $n_l$ repetitions of the RIPSP generate a desired overall rotation $\Theta_{\text{target}}$. This calculation indicates that $\tau_1$ and $\tau_2$ should be chosen such that $16 \cot(2\pi J_{IS}\tau_2) = 3 \cot(2\pi J_{IS}\tau_1)$ for an $IS$ spin system, which in the limit that $2\pi J_{IS}\tau_1 \ll 1$ where $2\pi J_{IS}\tau_2 \ll 1$, becomes $16\tau_1 = 3\tau_2$. Substituting this relationship into the constraint that $\Theta_{\text{target}} = n_l\Theta_{\text{RIPSP}}$ then gives:

$$
\tau_1^{\text{opt.}} = \frac{3}{32\pi J_{IS}} \sqrt{\frac{\Theta_{\text{target}}}{3n_l\theta}}
$$

$$
\tau_2^{\text{opt.}} = \frac{1}{2\pi J_{IS}} \sqrt{\frac{\Theta_{\text{target}}}{3n_l\theta}}
$$

\begin{equation}
\text{(2.5)}
\end{equation}
From Equation 2.5, the conditions that \(2\pi J_{IS} \tau_1^{\text{opt.}} \ll 1\) and \(2\pi J_{IS} \tau_2^{\text{opt.}} \ll 1\) imply \(\Theta_{\text{target}} \ll 3n_t\theta\). Finally, the total excitation time for \(n_t\) repetitions of the RIPSP using the optimal times in Equation 2.5 is given by;

\[
T_{\text{exc.}}^{\text{RIPSP}} = n_t \tau_e^{\text{opt.}} = n_t \left( 64\tau_1^{\text{opt.}} + 12\tau_2^{\text{opt.}} \right) = \frac{12n_t}{\pi J_{IS}} \sqrt{\frac{\Theta_{\text{target}}}{3n_t\theta}} \tag{2.6}
\]

Applying \(n_t\) loops of the RIPSP sequence to the initial \(I\) spin \(\vec{z}\)-magnetization, \(\hat{I}_Z\), generates;

\[
\left( \hat{U}_{\text{RIPSP,}+} \right)^{n_t} \hat{I}_Z \left( \hat{U}_{\text{RIPSP,}+}^\dagger \right)^{n_t} = \hat{I}_Z \cos \left( n_t\Theta_{\text{RIPSP}} \right) \mp \sin \left( n_t\Theta_{\text{RIPSP}} \right) \hat{I}_Y \tag{2.7}
\]

By subtracting the \(^1\text{H}\) signal under \(\hat{U}_{\text{RIPSP,}+}\) from the \(^1\text{H}\) signal under \(\hat{U}_{\text{RIPSP,}-}\), an overall signal proportional to \(2\sin(n_t\Theta_{\text{RIPSP}})\) is generated. This subtraction, does not reduce sensitivity of the \(^{13}\text{C}\)-satellite signal, but further reduces the already small unwanted \(^1\text{H}\) signal from molecules without a \(^{13}\text{C}\) spin, since the \(^1\text{H}\) spins in these molecules experience identical evolutions under \(\hat{U}_{\text{RIPSP,}+}\).

### 2.2.2 Effects of Homonuclear Spin - Spin Coupling During the RIPSP Sequence

For \(I_nS\) spin systems, the effects of homonuclear spin-spin couplings during the RIPSP sequence can be ignored since all the \(I\) spins are magnetically equivalent. However, if the \(I\) spins are inequivalent, the effects of homonuclear \(I\) spin-spin couplings during the RIPSP must be considered. Due to the fact that the RIPSP pulse cycle time, \(\tau_e = 64\tau_1 + 12\tau_2\), can be on the order of tens of milliseconds and the fact that the \(I\) spins experience a series of \(\pi\) – pulses that are, in general, applied rapidly compared to the inverse of the differences in \(^1\text{H}\) chemical shifts, the initial excitation of \(^1\text{H}\) spins directly bound to a \(^{13}\text{C}\) spin can undergo TOCSY-like [46] transfers of the excitation mediated by \(^1\text{H}\)-\(^1\text{H}\) spin-spin couplings to other \(^1\text{H}\) spins within molecules containing a \(^{13}\text{C}\) spin.
The effective propagator for the RIPSP sequence, taken to the lowest order, and accounting for the effect of homonuclear spin-spin couplings, is given by:

$$\widehat{U}_{\text{RIPSP}} \pm = e^{-i2\pi n_1\tau_c \left( \sum_{j<k} J_{jk} \frac{\vec{I}_j \cdot \vec{I}_k}{2} + \sum_k v_{\text{EFF},k,\text{RIPSP}} \vec{I}_k \right)}$$  \hspace{1cm} (2.8)

where the strength of the effective field under the RIPSP that the $k$th $I$ spin experiences when $2\pi J_{k,IS} \tau_1 \ll 1$ and $2\pi J_{k,IS} \tau_2 \ll 1$ is given by:

$$v_{\text{EFF},k,\text{RIPSP}} \approx \frac{\Theta_{\text{RIPSP}}}{2\pi \tau_c} \frac{8\pi \theta J_{k,IS}^2 \tau_1 \tau_2}{16\tau_1 + 3\tau_2}$$  \hspace{1cm} (2.9)

where $J_{k,IS}$ is the heteronuclear scalar coupling between the $S$ and $k$th $I$ spin. It is interesting to compare the propagator under the RIPSP sequence in Equation 2.8 to propagator for a CPMG-INEPT pulse block [47, 48], where a series of $\pi$-pulses are applied simultaneously to both $I$ and $S$ spins in order to refocus chemical shift differences while recoupling the heteronuclear spin-spin coupling:

$$\widehat{U}_{\text{CPMG-INEPT}}(\tau_c) = e^{-i2\pi \tau_c \left( \sum_{j<k} J_{jk} \vec{I}_j \cdot \vec{I}_k + \sum_k J_{k,IS} \vec{I}_k \vec{S}_z \right)}$$  \hspace{1cm} (2.10)

The total time for the CPMG-INEPT pulse block is chosen to be $\tau_c = \frac{1}{2J_{\text{target}}}$ in order to efficiently transfer single-quantum $I$ spin coherence into heteronuclear antiphase $I$ spin coherence for $I$ spins that are coupled to an $S$ spin with $J_{IS} = J_{\text{target}}$. In contrast, the RIPSP generates an effective field with phase $\hat{x}$ with strength $v_{\text{EFF},k,\text{RIPSP}}$ acting on the $k$th spin and no polarization transfer occurs between the $I$ and $S$ spins under the RIPSP propagator in Equation 2.8. When $|v_{\text{EFF},k,\text{RIPSP}} - v_{\text{EFF},j,\text{RIPSP}}| \gg |J_{jk}|$ for all $j$, negligible transfer of the excitation on the $k$th $I$ spin to the other $I$ spins occurs. However, when $|v_{\text{EFF},k,\text{RIPSP}} - v_{\text{EFF},j,\text{RIPSP}}| \leq |J_{jk}|$, the excitation on the $k$th $I$ spin is transferred to the other $I$ spins.

Simulations of the $I$ spin spectra after an initial excitation under the RIPSP sequence are shown in Figure 2.3 for a four spin system comprised of 3 $I$ spins and one $S$ spin. The simulations were performed using in house MATLAB [49] spin simulations. In the simulations, only the first $I$ spin was coupled to the $S$ spin (the spectral parameters used in the simulation are given in the caption of Figure 2.3.)
For the RIPSP sequence, different values of $\theta$ and $n_l$ were simulated but with the constraint that $n_l \theta = \frac{39.3136 \pi}{180}$ so that the RIPSP sequence would generate the same nominal rotation in the absence of $I-I$ spin-spin couplings of $n_l \Theta_{RIPSP} \approx \frac{97.8 \pi}{180}$ in all simulations. Additionally, either the exact propagator under the RIPSP sequence in Figure 2.3 using $\delta-$pulses on the $S$ spin but non, $\delta-$pulses on the $I$ spins [red spectra in Figure 2.1] or the AHT derived propagator in Equation 2.8 [blue spectra in Figure 2.3] were used in the simulations.

The AHT calculations and the exact numerical simulations were in excellent agreement as shown in Figure 2.3. In fact, as long as $2\pi n_l \tau, \nu^{EFF}_{k,RIPSP} \leq \pi$, Equation 2.8, was found to be a good approximation to the exact propagator under the RIPSP pulse sequence. Since the only nonzero heteronuclear coupling in the simulations was $J_{1S}$, the RIPSP sequence generates an excitation of the first $I$ spin ranging from approximately 100% for $n_l = 1$ to approximately 60% for $n_l = 8$. The amount of excitation on the heteronuclear coupled $I$ spin is related to the strength of the effective field under the RIPSP, $\nu^{EFF}_{1,RIPSP}$ in Equation 2.9. For $\nu^{EFF}_{1,RIPSP} \geq |J_{13}| = 4.35$ Hz, the first $I$ spin was almost fully excited. As $\nu^{EFF}_{1,RIPSP}$ decreased below $J_{13} = 4.35$ Hz, the excitation of the first $I$ spin decreased as the amount of excitation found on the other $I$ spins increased. This was due to an excitation transfer mediated by the $I-I$ spin-spin couplings during the RIPSP sequence. As seen in Figure 2.3, partially dispersive lineshapes were also observed for the exact simulations (red) as $\nu^{EFF}_{1,RIPSP}$ decreased. This was due to higher-order contributions to the AHT from the $I-I$ spin-spin coupling during the RIPSP sequence that are neglected in Equation 2.8. In practice, purely absorptive spectra can be obtained by applying a $z$-filter [45] after application of the RIPSP as shown in Figure 2.1. In this case, the phases of the $\frac{\pi}{2}$ pulses are $\pm X$ since the transverse magnetization after the RIPSP should be mostly along the $\hat{y}-$direction [Eq. 2.7]. Experiments which apply $z$-filters with the RIPSP to generate absorptive spectra are shown in Figure 2.2.
Figure 2.3: Simulations of the effects of homonuclear spin-spin couplings during an RIPSP sequence in a four-spin system (three $I$ spins and one $S$ spin) with the following spectral parameters: $\nu_{I1} = \nu_S = 0$ Hz, $\nu_{I2} = 297$ Hz, $\nu_{I3} = 401$ Hz, $J_{1,IS} = 150$ Hz, $J_{2,IS} = J_{3,IS} = J_{12} = 0$ Hz, $J_{13} = 4.35$ Hz, and $J_{23} = -10.1$ Hz. The simulated 90-acquire spectrum [black, $\tilde{\rho}(0) = I_Y$] and spectra after excitation under the RIPSP [red and blue, $\tilde{\rho}(0) = \tilde{I}_{RIPSP,\delta}$] are shown. The parameters for the RIPSP sequence were $\tau_1 = 250 \mu$s, $\tau_2 = 700 \mu$s, and $n_l \theta = 39.336 \pi$ for $n_l = 1$, $n_2 = 2$, $n_l = 4$, and $n_l = 8$. The propagator, $\tilde{U}_{RIPSP,\delta}$, was evaluated using either exact numerical simulation (red, with $\delta-$pulses applied to the $S$ spin and non-$\delta$ pulses applied to the $I$ spins with $\frac{\omega_{\text{RF}}}{2\pi} = 35.7$ kHz) or by using (blue) the AHT propagator in Eq. 2.8. With this choice of parameters, $n_l\Theta_{\text{RIPSP}} \approx \frac{97.8\pi}{180}$ in all simulations. As $n_l$ increased and $\theta$ decreased, the effective field strength under the RIPSP sequence for the first $I$ spin, $\nu_{1,\text{RIPSP}}^{\text{EFF}}$, in Equation 2.9, decreased, resulting in increased excitation of the $I$ spins not coupled to the $S$ spin. When $\nu_{1,\text{RIPSP}}^{\text{EFF}} \ll |J_{13}|$, the signals from all $I$ spins were roughly equal.
2.3 Materials and Methods

2.3.1 Experimental

Experiments were performed using 5 mm CDCl$_3$ susceptibility matched Shigemi tubes (Shigemi, Inc.) with sample heights of approximately 1 cm (in order to reduce the effects of field inhomogeneities) as well as conventional 5 mm tubes (Norell, Inc.). Experiments were performed either on a 500 MHz Avance Bruker spectrometer (static magnetic field of 11.7 T with an operating frequency for $^1$H of 500.062 MHz) using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe [results are shown in Figure 2.4(C), Figure 2.5, and Figure 2.6] or on a 300 MHz Avance Bruker spectrometer (static field strength of 7 T with an operating frequency of $^1$H 300.13 MHz) equipped with a 5 mm Bruker BBI probe [results are shown in Figures 2.4(A) and 2.4(B)]. An optional z-filter [45] consisting of a smoothed chirp pulse calculated using Topspin’s pulse shape tool with a sweep width of 20 kHz, pulse length of 50 ms, and consisting of 10k points was used when specified.

The nutation curves under the RIPSP sequence in Figure 2.4 were acquired for the following three solutions: 5% solutions by volume of $^{13}$CHCl$_3$ (99% labeled, Cambridge Isotopes Laboratory (CIL), Inc.) in CDCl$_3$ (99.8 % labeled, (CIL)), $^{13}$CH$_2$Cl$_2$ (99% labeled, (CIL)) in CDCl$_3$, and $^{13}$CH$_3$C$_6$H$_5$ (99% labeled, Sigma-Aldrich, Inc.) in CDCl$_3$. Comparisons of the $^1$H spectrum after application of the RIPSP sequence with and without the z-filter [in this case, the maximum RF strength of chirped pulse was 2 kHz, sine bell pulsed field gradients were used during the 50 ms chirped pulse with $G_{chirp} = 3.8$ G/cm along with a 500$\mu$s crusher gradient with $G_{cr} = 17.1$ G/cm] were performed on a 0.884 M solution of 2,3-dibromopropionic acid (DBPA, Sigma Aldrich, Inc., 98% pure) in CDCl$_3$ that was doped with chromium(III) acetylacetonate (Sigma-Aldrich, Inc.) to a concentration of [Cr(acac)$_3$] = 0.004 M. These results are shown in Figure 2.9.

Spectra acquired using an RIPSP with z-filter sequence for Figure 2.6 a 0.17 M solution of brucine (anhydrous, 98% pure, Sigma-Aldrich, Inc.) in CDCl$_3$ and in
Figure 2.5 a 0.27 M solution of DBPA (98% pure, Sigma-Aldrich, Inc.) in CDCl$_3$ were also compared to the $^{13}$C-edited $^1$H spectra obtained using the following pulse sequences: the linear $^{13}$C-based $^1$H ($\Theta = \frac{\pi}{2}$) excitation sequence, a gradient echo 1D $^1$H-$^{13}$C HSQC sequence with a $^{13}$C CLIP [50] pulse applied prior to acquisition, the reverse INEPT sequence with $^1$H presaturation [30], a sensitivity enhanced gradient echo 1D $^1$H-$^{13}$C HSQC sequence [51] with $^{13}$C CLIP pulse, and a $^{13}$C-edited spin echo [52] with $^{13}$C CLIP pulse. The pulse sequence diagrams for these experiments is shown in Figure 2.7. Other relevant experimental parameters are given in the captions of Figures 2.4 - 2.6.

2.4 Results and Discussion

As described in Section 2.2, the RIPSP sequence in Figure 2.1 generates a pure $I$ spin rotation about the $\hat{x}$–axis in $I_nS$ spin systems when $2\pi J_{IS} \tau_1 \ll 1$ and $2\pi J_{IS} \tau_2 \ll 1$. Experimental demonstrations of the rotational properties of the $\hat{U}_{RIPSP}$ propagator are shown in Figure 2.4 for $IS$ [Fig. 2.4(A), $^{13}$CHCl$_3$], $I_2S$ [Fig. 2.4(B), $^{13}$CH$_2$Cl$_2$], and $I_3S$ [Fig. 2.4(C), $^{13}$CH$_3$C$_6$H$_5$] spin systems. In Figure 2.4, the spectra after $n_l$ applications of the RIPSP pulse block was measured for the following initial conditions: (red) $\hat{\rho}(0) = \hat{I}_X$, (blue) $\hat{\rho}(0) = \hat{I}_Z$, and (green) $\hat{\rho}(0) = -\hat{I}_Y$. The experimental nutations in the $I_nS$ spin systems were also fit to the formulas (blue) $\sin(n_l \Theta_n) e^{-\lambda_n n_l}$, (green) $\cos(n_l \Theta_n) e^{-\lambda_n n_l}$, and (red) $p_n e^{-\gamma_n n_l} + b_n$, where the asterisks denote evaluations of these expressions at a particular $n_l$, which are connected by solid lines. As can be seen in Figure 2.4, the RIPSP sequence does generate a nutation about the $\hat{x}$–axis in $I_nS$ spin systems. This is demonstrated in the initial $\hat{z}$– and $\hat{y}$–magnetization which underwent a nutation while the initial $\hat{x}$–magnetization simply decayed. The selectivity of the nutation based on the presence of a nonzero $^{13}$C-$^1$H coupling is visible in Figure 2.4(A) for $\hat{\rho}(0) = -\hat{I}_Y$ (green), where the residual, unlabeled $^{12}$CHCl$_3$ resonance does not nutate whereas the $^{13}$CHCl$_3$ resonances do. Note also that for $\hat{\rho}(0) = \hat{I}_Z$ [Fig.2.4(A), blue], the $^{12}$CHCl$_3$ resonance was not
excited. Finally, when comparing the nutations in the $IS$, $I_2S$, and $I_3S$ spin systems, the nutation appears to decay most quick in the $I_3S$ system and the slowest in the $IS$ spin system. The origin of this increased dampening of the nutations in an $I_3S$ spin system compared to an $IS$ spin system can be thought of as arising from higher-order contributions to the average Hamiltonian under the RIPSP sequence that do not generate a pure rotation [see, for example, Eq. 2.4]. Simulations also demonstrate that the nutations in $I_2S$ and $I_3S$ spins systems are more sensitive to imperfections in the $I$ spin pulses, which may be due to pulse miscalibrations and/or RF inhomogeneity, compared to the nutations in an $IS$ spin system.

Since the RIPSP sequence primarily excites only $^1H$ spins coupled directly or indirectly (via $^1H$-$^1H$ spin-spin couplings) to a $^{13}C$ spin, the spectra obtained after application of the RIPSP sequence [especially with subtraction of the spectra under $\hat{U}_{RIPSP,+}$ and $\hat{U}_{RIPSP,-}$ in Equation 2.7] are essentially $^{13}C$-edited $^1H$ spectra. In as much, the $^{13}C$-edited $^1H$ spectra using the RIPSP with z-filter in Figure 2.5, DBPA in Figure 2.6 and brucine solutions in CDCl$_3$ were compared to the pulse sequences in Figure 2.7 that also generate $^{13}C$-edited $^1H$ spectra.

Linear $^{13}C$-based $^1H$ excitation with an additional $^{13}C$ CLIP pulse applied before acquisition in order to remove heteronuclear antiphase single-quantum $I$ spin coherence that arises due to J-mismatch of the delays. Details of this pulse sequence are given in Figure 2.7, the reverse INEPT sequence with $^1H$ presaturation [30], the gradient echo 1D $^1H$-$^{13}C$ HSQC with CLIP pulse (based on the Bruker pulse sequence “hsqcgpnd1d”), $^{13}C$-edited spin-echo [52] with CLIP pulse, and sensitivity enhanced gradient echo 1D $^1H$-$^{13}C$ HSQC with CLIP pulse where the pulse delays were chosen to enhance the sensitivity for $IS$ spin pairs [51].

The $^{13}C$-edited spin echo with CLIP pulse, shown in Figure 2.7(B), was the most sensitive of all the sequences used in both Figures 2.5 for DBPA and Figure 2.6 for brucine. In these examples, a lower receiver gain was used in order to avoid baseline and peak distortions resulting from the subtraction of unwanted $^1H$ signal in non-$^{13}C$ containing molecules under the sequence. Most of the other sequences used in Figure
Figure 2.4: $\tilde{U}_{\text{RIPSP}}$, in Figure 2.1, applied to solutions of (A) $^{13}$CHCl$_3$ in CDCl$_3$ (5% by volume), (B) $^{13}$CH$_2$Cl$_2$ in CDCl$_3$ (5% by volume), and (C) $^{13}$CH$_3$C$_6$H$_5$ in CDCl$_3$ (5% by volume) as a function of the RIPSP loop number, $n_l$, applied to (red) $\tilde{\rho}(0) = \tilde{I}_X$, (blue) $\tilde{\rho}(0) = \tilde{I}_Z$, and (green) $\tilde{\rho}(0) = -\tilde{I}_Y$. Initial $\tilde{x}$—magnetization was spin-locked (red), whereas initial $\tilde{y}$— and $\tilde{z}$—magnetizations underwent nutations. In all experiments, $N_s = 16$, $d_1 = 30\mu$s, and both the $^1$H and $^{13}$C RF transmitters were applied on resonance. In (A), $\tau_1 = 200\mu$s and $\tau_2 = 500\mu$s, in (B), $\tau_1 = 170\mu$s and $\tau_2 = 750\mu$s, and in (C), $\tau_1 = 292\mu$s and $\tau_2 = 900\mu$s. The following fits of the experimental nutations to damped oscillations were found (asterisks denote evaluations of the fits at each value of $n_l$ with solid lines connecting these points): (A) In chloroform, (blue) $\sin(n_l\Theta_1)e^{-0.06n_l}$, (green) $\cos(n_l\Theta_1)e^{-0.06n_l}$, and (red) $e^{-0.02n_l}$ where $\Theta_1 = 16\theta\sin(2\pi J_{IS}\tau_1)\sin(2\pi J_{IS}\tau_2) \approx \frac{29\pi}{180}$ with $J_{IS} = 209$ Hz. (B) In dichloromethane, (blue) $\sin(n_l\Theta_2)e^{-0.11n_l}$, (green) $\cos(n_l\Theta_2)e^{-0.11n_l}$, and (red) $0.3e^{-0.4n_l} + 0.65$ where $\Theta_2 = 4\theta\sin(4\pi J_{IS}\tau_1)\sin(2\pi J_{IS}\tau_2) \approx \frac{28.9\pi}{180}$ with $J_{IS} = 177$ Hz. (C) In $\alpha$–$^{13}$C labeled toluene, (blue) $\sin(n_l\Theta_3)e^{-0.24n_l}$, (green) $\cos(n_l\Theta_3)e^{-0.24n_l}$, and (red) $0.9e^{-0.02n_l}$ where $\Theta_3 = 16\theta\sin(2\pi J_{IS}\tau_1)\cos^2(2\pi J_{IS}\tau_1)\sin(2\pi J_{IS}\tau_2) \approx \frac{39.5\pi}{180}$ with $J_{IS} = 127$ Hz.
Figure 2.5: Spectra were acquired on a 500 MHz Avance spectrometer for a 0.27 M DBPA solution in CDCl₃ [in all spectra, N_s = 128, d₁ = 1 s, acquisition time of 5 s, \( \frac{\omega_{1\text{H}}}{2\pi} = 11.6 \text{ kHz} \), \( \frac{\omega_{13\text{C}}}{2\pi} = 32 \text{ kHz} \), and the \(^1\text{H}\) and \(^{13}\text{C}\) RF transmitters were set at 4.511 ppm and 40 ppm, respectively], and a nominal \( J_{1S} = 161 \text{ Hz} \) was used in calculating the delays for many of the sequences. All spectra are plotted on the same scale and zoomed in by the factors denoted in the Figure. Details of all the pulse sequences given in Figures 2.1 and 2.7. (A) 90-acquire spectrum with \(^1\text{H}\) assignments for reference. (B) Linear \(^{13}\text{C}\)-based \(^1\text{H}\) excitation \( [\Theta = \frac{\pi}{2}] \) with CLIP pulse. (C) Reverse INEPT with \(^1\text{H}\) presaturation. A continuous wave \(^1\text{H}\) presaturation pulse was applied during \( d₁ = 1 \text{ s} \) with strength \( \frac{\omega_{\text{presat}}}{2\pi} = 12.7 \text{ kHz} \). (D) Gradient echo 1D \(^1\text{H}-^{13}\text{C}\) HSQC with CLIP pulse. The pulsed field gradients had sine bell shapes with pulse lengths of \( p_{16} = 900 \mu\text{s} \) and strengths \( G₁ = 28 \text{ G/cm} \), \( G₂ = 7.035 \text{ G/cm} \) and \( G₃ = -10.5 \text{ G/cm} \). A gradient stabilization delay of \( d₁₆ = 400 \mu\text{s} \) was used. (E) \(^{13}\text{C}\)-edited spin echo with CLIP pulse. (F) Sensitivity-enhanced gradient echo 1D \(^1\text{H}-^{13}\text{C}\) HSQC with CLIP pulse. (G) RIPSP with z-filter using \( \tau₁ = 200 \mu\text{s} \), \( \tau₂ = 600 \mu\text{s} \), \( nₖ = 1 \), \( \theta = \frac{16\pi}{45} \), a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, \( G_{\text{chirp}} = 1.05 \text{ G/cm} \) and a 1 ms crusher gradient of strength \( G_{cr} = 5.25 \text{ G/cm} \).
Figure 2.6: acquired on a 500 MHz Avance spectrometer for a 0.17 M brucine solution in CDCl₃ [in all spectra, \( N_z = 128 \), \( d_1 = 1 \) s, acquisition time of 5 s, \( \omega_{\text{1H-C}} = 11.9 \) kHz, \( \omega_{\text{1H}} = 31.45 \) kHz, and the \(^1\)H and \(^{13}\)C RF transmitters were set at 4 ppm and 40 ppm, respectively]. A nominal \( J_{1S} = 145 \) Hz was used in calculating the delays for many of the sequences. All spectra are plotted on the same scale and zoomed in by the factors denoted in the Figure. Details of all the pulse sequences given in Figure 2.2. (A) 90-acquire spectrum and \(^1\)H assignments for reference. (B) Linear \(^{13}\)C-based \(^1\)H excitation \([\Theta = \pi/2]\) with CLIP pulse. (C) Reverse INEPT with \(^1\)H presaturation. A continuous wave \(^1\)H presaturation pulse was applied during \( d_1 = 1 \) s with strength \( \omega_{\text{presat}} = 12.5 \) kHz. (D) Gradient echo 1D \(^1\)H-\(^{13}\)C HSQC with CLIP pulse. The pulsed field gradients had sine bell shapes with pulse lengths of \( p_{16} = 900 \) µs and strengths \( G_1 = 28 \) G/cm, \( G_2 = 7.035 \) G/cm and \( G_3 = -10.5 \) G/cm. A gradient stabilization delay of \( d_{16} = 400 \) µs was used. (E) \(^{13}\)C-edited spin-echo with CLIP pulse. (F) Sensitivity-enhanced gradient echo 1D \(^1\)H-\(^{13}\)C HSQC with CLIP pulse. (G) RIPSP with z-filter using \( \tau_1 = 200 \) µs, \( \tau_2 = 600 \) µs, \( n_l = 1 \), \( \theta = 16\pi \), a 50 ms chirped pulse with a maximum RF amplitude of 4 kHz, \( G_{chirp} = 1.4 \) G/cm and a 1 ms crusher gradient of strength \( G_{cr} = 7 \) G/cm.
Figure 2.7: Pulse programs used for comparison with the RIPSP sequence with z-filter. Corresponding spectra for these experiments is found in Figures 2.5 and 2.6. In all cases, $\tau = \frac{1}{8J_{\text{HS}}}$. (A) The reverse INEPT with $^1\text{H}$ presaturation [30]. (B) $^{13}\text{C}$-edited spin echo experiment [52]. (C) Gradient echo 1D $^1\text{H}-^{13}\text{C}$ HSQC with CLIP [50] pulse applied to the $^{13}\text{C}$ spin before detection. Pulsed field gradient lengths were equivalent to the pulse width of $p_{16}$ with relative strengths of $G_1:G_3:G_2 = 80:-30:20$. $\tau$ were used to select $^1\text{H}$ single-quantum coherence that pass through $^{13}\text{C}$ single-quantum coherence. The pulse phases were $\phi = 11113333$, $\phi_2 = 00022$, $\phi_3 = 02$ and $\phi_4 = 02022020$. $\Delta_1 = p_{16} + d_{16}$ where $d_{16}$ is a gradient stabilization delay, $\delta = 4\mu\text{s}$, and $\Delta_2 = \Delta_1 + \delta$. (D) Linear $^{13}\text{C}$-based $^1\text{H}$ excitation that generates a pure $I$ rotation of angle $\Theta$ about the $\hat{x}$-axis in $I_{n'S}$ spin systems. Experiments with reversed phases of the $\phi$ and $\phi/2$ I spin pulses are subtracted from one another to generate $^{13}\text{C}$-edited $^1\text{H}$ spectra.
2.5 and Figure 2.6 can be run at higher receiver gains without significant spectral distortions as result of the decreased magnitude of the unwanted $^1$H signal prior to detection due to either gradient dephasing (as used in the gradient echo HSQC sequences), $^1$H presaturation (used in the reverse INEPT experiment), or simply from the small excitation of the unwanted $^1$H signal (as in the RIPSP sequence). The relative sensitivity of $^{13}$C-edited $^1$H spectra obtained from the pulse sequences used in Figure 2.5 and Figure 2.6 is compared to that obtained using the $^{13}$C-edited spin echo with CLIP sequence. It should be noted that the comparisons in brucine consider all $^1$H resonances except for protons 1, 4, 12, and 22 as shown in Figure 2.6(A), which, in general, were not significantly excited.

The reverse INEPT sequence with $^1$H presaturation Figure 2.7(A) was the least sensitive under the conditions studied in this work, where the intensities of the $^{13}$C satellites ranged from only 8%–11% and 10%–40% of that observed in the $^{13}$C-edited spin-echo displayed in Figure 2.5(C) vs. Figure 2.5(E) for DBPA and Figure 2.6(C) vs. Figure 2.6(E) for brucine, respectively. However, the use of $^1$H presaturation (which was confirmed by measuring the transverse and $\tilde{z}$-magnetization after the presaturation pulse) significantly suppressed the unwanted $^1$H signal while at the same time generating an NOE enhancement for some of the resonances in brucine (there did not appear to be any significant NOE enhancement in DBPA). The low sensitivity in these experiments was likely due to the short pulse duty cycle used in the experiments ($d_1 = 1$ s and $\tau_{acq} = 5$ s) and the long $T_1$ times of the $^{13}$C resonances.

For the linear $^{13}$C-based excitation with CLIP pulse [Fig. 2.7(D)] a nominal $\Theta = \frac{\pi}{2}$ rotation of those $^1$H spins coupled to a $^{13}$C is generated in half of the scans, which is subsequently subtracted from the signal with no nominal $\Theta = \frac{\pi}{2}$ excitation of the $^{13}$C-satellites in order to remove the unwanted $^1$H signal. In this case, the peak heights of the $^{13}$C satellites ranged from 30%–40% and 56%–68% of that observed using the $^{13}$C-edited spin-echo in Figure 2.5(B) vs. Figure 2.5(E) for DBPA and Figure 2.6(B) vs. Figure 2.6(E) for brucine, respectively.
In the gradient echo 1D $^1$H-$^{13}$C HSQC with CLIP pulse shown in Figure 2.7(C) only half of the $^{13}$C single-quantum coherence survives selection by pulsed field gradients. In this case, the peak heights of the $^{13}$C satellites ranged from approximately 30\% and 37\% – 42\% of that observed for the $^{13}$C-edited spin echo in Figure 2.5(D) vs. Figure 2.5(E) for DBPA and Figure 2.6(D) vs. Figure 2.6(E) for brucine, respectively. Part of the loss in sensitivity due to gradient selection can be recovered by additionally refocussing the other component of $^{13}$C spin coherence [51]. For the sensitivity enhanced gradient echo 1D $^1$H-$^{13}$C HSQC with CLIP pulse [Fig. 2.7(E)], the delays were chosen to enhance the signal for $^1$H-$^{13}$C spin pairs. In DBPA, the peak heights for the $^{13}$C-satellites associated with resonance $C$ in DBPA [see Fig. 2.5(A)] was approximately 86\% of what was obtained using a $^{13}$C-edited spin echo, whereas the other $^1$H resonances were approximately 34\% – 38\% of that observed using a $^{13}$C-edited spin echo [Fig. 2.5(F) vs. Fig. 2.5(E)]. In brucine, the peak heights of the $^{13}$C satellites ranged from 37\% – 56\% of that observed using a $^{13}$C-edited spin echo [Fig. 2.6(F) vs. Fig. 2.6(E)].

For the RIPSP with z-filter in Figure 2.1, the peak heights of the $^{13}$C satellites ranged from 67\% – 74\% and 69\% – 84\% of that observed for the $^{13}$C-edited spin echo in Figure 2.5(G) vs. Figure 2.5(E) in DBPA and Figure 2.6(G) vs. Figure 2.6(E) in brucine, respectively. The predicted maximum excitation expected under the RIPSP sequence should range from 93\% – 99\% in brucine ($J_{IS} = 145$ Hz) and 89\% – 100\% in DBPA ($J_{IS} = 161$ Hz).

However, relaxation during the RIPSP with a 50 ms z-filter, field inhomogeneities, and spin diffusion mediated by $^1$H-$^1$H spin-spin coupling can attenuate the expected excitation of the $^{13}$C-satellites. For DBPA, the $^{13}$C-edited $^1$H spectra was quantitative [see Fig. 2.2 and Table 2.1], but for brucine, however, excitation of certain $^1$H resonances [such as protons 1, 4, and 22 in Fig. 2.6(A)] was not significant. The lack of excitation for these $^{13}$C-satellites was due in part to $^{13}$C off-resonance effects, where the $^{13}$C-satellites corresponding to the 1, 4, and 22 $^1$H resonances were 65.1 ppm, 61.1 ppm, and 87.1 ppm off-resonance from the applied $^{13}$C RF at 40 ppm.
Another important factor for the small excitation of these $^{13}$C-satellites under the RIPSP was that the predicted maximum excitation should be between 84% – 90% since $J_{IS} \approx 160 - 165$ Hz for these $^{13}$CH spin pairs. For all other $^{13}$C-satellites in brucine, $J_{IS} \in [120 \, \text{Hz}, 150 \, \text{Hz}]$; as such, the maximum excitation under the RIPSP for $^{13}$CH spin pairs should be between 92% – 98% for the parameters used in Figure 2.6(G). For $^{13}$CH$_2$ and $^{13}$CH$_3$ spin pairs, the excitation under the RIPSP was between 80% – 100% over a wide range of $J_{IS}$ values. In DBPA, long-range $^2J_{IS}$ couplings can be observed in the $^1$H signal that was generated by $^1$H-$^1$H spin-spin coupling during the RIPSP. This signal is observable due to the excellent suppression of the unwanted $^1$H signal in non $^{13}$C-containing molecules.

Shigemi tubes (Shigemi, Inc) are commonly used to reduce the effects of static field ($B_0$) inhomogeneity. These tubes restrict the sample into a small volume of approximately 1 cm in height and the glass itself is susceptibility matched to the deuterated solvent being used. When spectra comparing experiments in which a Shigemi tube or conventional NMR tube is used [Fig. 2.8] it can be seen that the resonances were slightly broader when the sample is evaluated in the regular tube. The relative intensities for $^1$H spins that were not directly bonded to a $^{13}$C spin compared to the $^{13}$C-satellites were larger in a conventional tube than in a Shigemi tube, especially for the $^{13}$C-edited spin echo experiment [Fig. 2.8]. The results were similar, however, for both the sensitivity-enhanced gradient echo 1D $^1$H-$^{13}$C HSQC with CLIP pulse [Fig. 2.8(middle)] and the RIPSP with z-filter [Fig. 2.8(bottom)], indicating that field inhomogeneities did not significantly affect the performance of these sequences. The intensities of the $^{13}$C-satellites under the RIPSP with z-filter were 26% – 33% smaller in the Shigemi tube and approximately 25% – 33% smaller in the regular tube than that observed using the $^{13}$C-edited spin echo sequence. For the sensitivity enhanced HSQC, the intensities of the $^{13}$C-satellites were from roughly 14% (proton C) to 62% – 66% (protons A and B) smaller in the Shigemi tube, and approximately 23% (proton C) and 66% (protons A and B) smaller in the conventional NMR tube compared to those signals observed for the $^{13}$C-edited spin echo. For longer
loops of the RIPSP sequence \((nl >> 1)\), both RF and \(B_0\) inhomogeneity can affect the spectra in the RIPSP sequence due to the large number of pulses that are used.

As mentioned earlier, bilinear pulses are commonly used to perform selective excitation of \(I\) spins that are coupled to an \(S\) spin. When \(\tau = \frac{2m+1}{2J_{IS}}\) for integer \(m\), \(\hat{U}_{\text{linear}}(\tau, \Theta) = \hat{P}_X^I(\Theta)\) (for an \(I_nS\) spin system, \(e^{-4\pi i\hat{I}_Z\hat{S}_Z} = (-1)^n\hat{I}\) where \(\hat{I}\) is the identity operator). For both the bilinear and linear sequences, \(\tau\) must be set to \(\tau = \frac{2m+1}{2J_{IS}}\) for integer \(m\) in order that a bilinear/linear rotation of the \(I\) spins is generated. For a distribution of coupling constants, the so-called “J-mismatch” occurs, and pure bilinear/linear rotations will not be generated when \(\tau \neq \frac{2m+1}{2J_{IS}}\) for integer \(m\). An optional CLIP pulse [50] can be applied to the \(S\) spin in order to transform heteronuclear single-quantum coherences into undetectable heteronuclear multiple-quantum coherences and thus remove the heteronuclear antiphase signal.

In Figure 2.9, the RIPSP sequence was applied to a DBPA solution in CDCl\(_3\) doped with Cr(acac)\(_3\) to examine the effects of applying a z-filter at the end of the RIPSP sequence. In Figure 2.9(A), the 90-acquire spectrum (top) for the DBPA solution is displayed, along with the spectra under the propagator \(\hat{U}_{\text{RIPSP},-}\) from a RIPSP sequence with [Fig. 2.9(A), bottom] and without [Fig. 2.9(A), middle] a z-filter (no subtraction of the signal obtained from \(\hat{U}_{\text{RIPSP},+}\) was performed). In this case, the excitation of the \(^1\text{H}\) signal in non \(^{13}\text{C}\)-containing molecules was approximately 3.1% under the RIPSP sequence without the z-filter [Fig. 2.9(A), middle] and 1.6% with the z-filter [Fig. 2.9(A), bottom]. The majority of the \(^1\text{H}\) signal in non \(^{13}\text{C}\)-containing molecules, however, was due to the interference between the \(^1\text{H}-^1\text{H}\) spin couplings and \(^1\text{H}\) chemical shift differences during the RIPSP sequences, which is the origin of this small unwanted \(^1\text{H}\) signal. As discussed in Section 2.2, subtracting the \(\hat{U}_{\text{RIPSP},+}\) signal from the \(\hat{U}_{\text{RIPSP},-}\) signal removes the unwanted \(^1\text{H}\) signal in non \(^{13}\text{C}\)-containing molecules while the \(^1\text{H}\) signal from \(^{13}\text{C}\)-containing molecules adds, thereby avoiding a reduction in sensitivity per scan. Note that the unwanted \(^1\text{H}\) signals that are subtracted using the RIPSP sequence are never greater than 3% – 5% of the \(^1\text{H}\) signal from a \((\frac{\pi}{2})\) –acquire experiment. The smallness of the unwanted \(^1\text{H}\) not only results
Figure 2.8: Comparison of the spectra in DBPA using (top) the $^{13}$C-edited spin echo with CLIP pulse, (middle) sensitivity enhanced gradient echo 1D $^1$H-$^{13}$C HSQC with CLIP and the (bottom) RIPSP with z-filter sequences in either a 5 mm Shigemi tube (left) or a conventional 5 mm NMR tube (right). Experimental parameters in the Shigemi tube are given in Figure 2.5. For the conventional NMR tube, the RF powers were slightly smaller, $\omega_{1H}/2\pi = 30.846$ kHz and $\omega_{13C}/2\pi = 11.11$ kHz. The gradients used with the z-filter were $G_{chirp} = 1.8$ G/cm and $G_{cr} = 9$ G/cm. The receiver gain was set at either RG=9 for experiments performed in the Shigemi tube or RG=35.9 using conventional tubes, respectively. The spectra have been plotted on the same scale for each tube.
in a substantial reduction of subtraction errors but also allows for the receiver gain to be set at higher levels when using the RIPSP sequence when compared to other editing sequences, thus providing better sensitivity per scan without affecting the suppression of the unwanted $^1\text{H}$ signal.

The subtracted signals are shown in Figure 2.9(B), without [Fig. 2.9(B) top] and with [Fig. 2.9(B) bottom] the application of a z-filter [the RIPSP parameters were $n_t = 1$, $\theta = \frac{51.43\pi}{180}$, $\tau_1 = 150\mu s$, $\tau_2 = 600\mu s$, $N_s = 128$, and $d_1 = 5s$]. In Figure 2.95(B) (top), the $^1\text{H}$ signals from directly bound $^{13}\text{C}$ nuclei were mostly absorptive while the signal for $^1\text{H}$ resonances that were not directly bound to a $^{13}\text{C}$ nucleus were slightly dispersive. The spectrum can be made to be absorptive by application of the z-filter before detection, as shown in Figure 2.9(B) (bottom). In the resulting spectrum, $^2J_{CH}$ couplings were clearly visible in the $^1\text{H}$ signals located between the dominant $^{13}\text{C}$-satellite signals. In Figure 2.9(B), a $60\% - 73\%$ excitation of the $^{13}\text{C}$-satellite signals was observed with a suppression of the unwanted $^1\text{H}$ signal from non $^{13}\text{C}$-containing molecules being greater than $99.9\%$. The observed excitation was somewhat lower than the maximum excitation predicted for an $IS$ spin system, which for the parameters used in Figure 2.9, should be $\sin \left( \Theta_1 \right) = \sin \left(16\theta \sin(2\pi J_{IS}\tau_1) \sin(2\pi J_{IS}\tau_2)\right) \approx 94\%$ using $J_{IS} = 161\text{ Hz}$. This discrepancy can be accounted for by two factors: magnetization transfer via $^1\text{H}-^1\text{H}$ spin couplings and relaxation during the RIPSP sequence [for the RIPSP used in Fig. 2.9, $\tau_c = 16.8\text{ms}$]. To confirm this, numerical simulations of the spectra under the RIPSP sequence on DBPA are also shown in Figure 2.9(B) [red spectra], where simulations of the two isotopomers of DBPA with the $^{13}\text{C}$ spin at either the 2 or 3 positions [Fig. 2.9(A)] were added. The following spectral parameters were also used in the simulations: $J_{a3} = 161\text{ Hz}$, $J_{a2} = -4\text{ Hz}$, $J_{b3} = 161\text{ Hz}$, $J_{b2} = -4\text{ Hz}$, $J_{c3} = -4\text{ Hz}$, $J_{c2} = 161\text{ Hz}$, $J_{ab} = -10.1\text{ Hz}$, $J_{ac} = 4.35\text{ Hz}$, $J_{bc} = 11.25\text{ Hz}$, $\delta_a = 3.71\text{ ppm}$, $\delta_b = 3.92\text{ ppm}$, $\delta_c = 4.51\text{ ppm}$, and a line broadening of $1.54\text{ Hz}$. Excellent agreement between the simulations and experimental results was observed in Figure 2.9(B).
Figure 2.9: Experiments were performed using a 0.884 M solution of DBPA in CDCl$_3$ that was doped with chromium (III) acetylacetone (Sigma-Aldrich) to a concentration of [Cr(acac)$_3$]=4 mM. (A) 90-acquire spectrum (top), and the spectra after excitation using the RIPSP sequence (with propagator given by $U_{RIPSP\_z}$) with (bottom) and without (middle) a $z$-filter applied before acquisition [50 ms smoothed chirped pulse with 20 kHz sweep width and maximum RF strength of 2 kHz, with sine-bell shaped pulsed field gradients with $G_{chirp} = 3.8$ G/cm and a 500 µs crusher gradient $G_{cr} = 17.1$ G/cm]. Note that subtraction of the signal under $U_{RIPSP\_z}$ was not performed. Compared to the 90-acquire spectrum, the $^1$H signal from non $^{13}$C-containing molecules was suppressed by approximately (bottom) 98.4% and (middle) 96.4% with and without the $z$-filter, respectively. (B) $^{13}$C-edited proton experimental (black) and simulated (red) spectra under the RIPSP sequence with (bottom) and without (top) $z$-filter. The suppression of unwanted proton signal from non $^{13}$C-containing molecules was greater than 99.9% whereas the excitation of the $^{13}$C-satellites ranged from 60% - 73%. Signals that arise at 4.5 ppm, 3.9 ppm, and 3.7 ppm represent the transfer of coherence to $^1$H spins not directly coupled to $^{13}$C by proton-proton spin-spin coupling. In all experiments, $N_s = 128$, $d_1 = 5s$, an acquisition time of 5s, and the RF transmitter offsets were set to 4.511 ppm for $^1$H and 40 ppm for $^{13}$C, respectively.
CHAPTER 3

Line narrowing observations under the RIPSP sequence

In chapter two a PSP based upon the reverse INEPT [30] pathway was applied to a series of $I_nS$ systems of increasing complexity. The effect of the RIPSP was demonstrated on $^{13}\text{C}$-labeled chloroform, methylene chloride, toluene and unlabeled 2,3-dibromopropionic acid and brucine. Experimental results in dibromopropionic acid revealed unexpected line narrowing in signals collected under the RIPSP as compared to the respective 90-acquire experiment. In this chapter, the line narrowing effect is explored in detail using $^{13}\text{C}$ labeled carbohydrate solutions, labeled chloroform and methylene chloride. Experimental outcomes indicate the presence of single-quantum multispin terms. We believe that lengthening of the free induction decay [FID], results in multispin order that generates terms that evolve into signal at later times, in analogy to highly polarized spin systems [16].

3.1 Background

In an ideal homogeneous static field the FID produced from an NMR sample would be expressed as $A[\exp(-\frac{t}{T_2}) \exp(j\omega_0 t)]$, where $A$ is the signal amplitude and $T_2$ is the transverse relaxation time [53]. This results in a Lorentzian line shape described according to Equation 3.1. However, inconsistencies in manufacturing of magnets combined with the influence of the sample on the RF field result in imperfections reflected in the lineshipe. The result is variation in the RF field over the sample
volume and shifts in Larmor frequency, \( \omega \), as a function of time.

\[
\mathcal{L}(\omega) = Re \left\{ \frac{AT_2}{[1 + jT_2(\omega - \omega_0)]} \right\} = \frac{AT_2}{1 + T_2^2(\omega - \omega_0)^2} \tag{3.1}
\]

Inside the bore of a superconducting magnet, the field can be described in terms of spherical harmonics [54],

\[
B_0 = \sum_{n=0}^{\infty} \sum_{m=0}^{n} C_{nm}(r^n a^{-n}) P_{nm}(\cos \theta, \cos(\phi - \psi_{nm})) \tag{3.2}
\]

where \( C_{nm} \) and \( \psi_{nm} \) are constants that can be manipulated to describe the circumstance under which the static magnetic field has no electric current running through it. The term \( a \) is the average magnetic field radius, and \( P_{nm}(\cos \theta) \) are polynomial functions in \( \cos \theta \). When \( m = 0 \), the \( P_n(\cos \theta) \) terms are referred to as the Legendre polynomials, which give rise to the zonal harmonics describing the zonal field and the condition for cylindrical symmetry in \( B_0 \). Equation 3.2 reduces to [54];

\[
B_0 = \sum_{n=0}^{\infty} C_{nm}(r^n a^{-n}) P_n(\cos \theta) \tag{3.3}
\]

The field along the \( z \)-axis can be derived from the zonal equation by setting \( \theta = 0 \), for which \( P_n(\cos \theta) = 1 \), giving rise to \( B_{0z-axis} = \sum_{n=0}^{\infty} C_{nm}(z^n a^{-n}) \) When these polynomials are the functions for which \( m \neq 0 \) and \( P_{nm}(\cos \theta) \), the are referred to as Legendre polynomials and contribute to the tesseral harmonics. Looking at Equation 3.2, note that the final cosine term imposes the condition of circular movement about the \( z \)-axis. The requirement for a perfectly homogeneous field is one in which \( n \) and \( m \) equal zero and the variables \( r, \theta \) and \( \phi \) do not change. In as much, the harmonics represented for all other conditions coincide with a perturbation to the magnetic field leading to induced inhomogeneity.

Mechanisms that cause line broadening are divided into two categories: inhomogeneous and homogeneous. Those processes contributing to inhomogeneous line broadening are the result of magnetic inequivalence between spins in a system [55]. The influence of these interactions is limited by the timescale of the FID and the signal arising from inhomogeneous broadening processes decay as a function of time.
The decay is dependent upon the transverse relaxation rates of components within the system and effects from sources of homogeneous line broadening. Homogeneous line broadening processes are responsible for shortening the lifetime of transitions between quantum states, or destroying coherence between states altogether [55]. Reducing the influence of homogeneous broadening mechanisms can improve spectra by eliminating some degree of signal overlap thus revealing spectral elements corresponding to coherent quantum processes associated with inhomogeneous broadening mechanisms.

The decay of the FID is described by Equation 3.4 and represents the solution to Bloch’s equation [Eq. 3.5] [56].

\[
S(t) = M_0 \sin \theta_0 \exp \left( \frac{t}{T_2^*} \right)
\] (3.4)

\[
\frac{d\mathbf{M}(t)}{dt} = \gamma \mathbf{M}(t) \otimes \mathbf{B}(t) - \mathbf{R} \left[ \mathbf{M}(t) - \mathbf{M}_0 \right]
\] (3.5)

The factor \(T_2^*\) is the dephasing time, or effective transverse relaxation time, \(\mathbf{R}\) is the relaxation matrix and \(\theta_0\) is the flip angle immediately following an RF pulse. The time domain FID is processed by Fourier transform to produce a spectrum in the frequency domain. Ideally, the lineshape in a liquid NMR experiment is Lorentzian and the linewidth can be measured as the width of a peak at half height, corresponding to \(\Delta \nu_0 = (\pi T_2) \, ^{-1}\). Fourier transformation of the decay envelope in Equation 3.4 gives;

\[
S(\omega) = M_0 \sin \theta_0 \frac{(T_2^*)^{-1}}{[(T_2^*)^{-2} + (\omega - \omega_0)]}
\] (3.6)

The value of \(T_2\) can be measured using CPMG spin-echo sequences [57, 58] or through spin locking experiments [58–60]. The PROJECT sequence [Figure 3.2] [60] uses “perfect spin echoes” to produce pure \(T_2\) weighted spectra. Since it is possible to mitigate the contribution of \(T_2\) line broadening using delayed acquisition, a technique for improving resolution in Fourier NMR by “filtering” broad signals that arise from species with fast \(T_2\) relaxation times [61–63], the PROJECT sequence can, therefore, be used to evaluate the contribution of homogeneous broadening processes to a spin system.
Line narrowing has also been seen in in highly polarized solids evolving under the dipolar Hamiltonian [16]. In this case, the high temperature limit, the condition $|\Delta E_{\beta\alpha}| \ll k_B T$, was abandoned and the generally ignored influence of multispin terms on the FID following RF excitation were included in models describing the spin system. [16].

### 3.2 Theory

NMR experiments of spin-$\frac{1}{2}$ liquids can be represented by a density matrix which defines the system according to the high temperature approximation [11]. In this picture, the Boltzmann distribution of populations between energy levels drive the evolution of the system. The time required to attain the Boltzmann distribution of populations between the Zeeman energy levels is on the order of the $T_2$ rate of the FID. At equilibrium $\hat{\rho}_0$ is given by;

\[
\hat{\rho}_0 \approx \frac{1}{2} \hat{1} + \frac{\Delta E_{\beta\alpha}}{2k_B T} \hat{I}_Z
\]

\[
= \frac{1}{2} \hat{1} + \hat{\rho}_{eq,red.}
\]

where $\hat{\rho}_{eq,red.}$ is the reduced density matrix and represents the deviation for a completely unpolarized spin system (in this case, the $\hat{z}$-magnetization generated by an energy difference between up and down spins). Under high external magnetic field the Zeeman energy dominates the terms in the system Hamiltonian, $\hat{H}_{sys}$, and the resulting energy between eigenlevels is assumed equal to the sum of the Zeeman and spin-spin energies. The total energy of the system is conserved by internal terms arising from flip-flop transitions, those spin-spin interactions of the type $I_+ I_- + I_- I_+ [11]$.

Recall from Chapter 2 that the effective Hamiltonian for the $\hat{U}_{RIPSP,\pm}$ propagator contains pure rotation terms in addition to multispin single- and triple-quantum terms due the reverse INEPT “pathway” used to construct the RIPSP [6,31]. For inequivalent $I$ spins, excitation of $^1H$ spins directly bound to a $^{13}C$ spin under the RIPSP can potentially undergo TOCSY-like [46] transfers of the excitation medi-
tated by $^1$H-$^1$H spin-spin couplings to other $^1$H spins within molecules containing a $^{13}$C spin. Accounting for these interactions the effective propagator [Chp.2, Eq.2.8] was 
\[ \hat{U}_{\text{RIPSP,}+} = e^{-i2\pi n_i c \left( \sum_{j<k} J_{jk} \hat{I}_j \cdot \hat{I}_k + \sum_k \nu_{k,\text{RIPSP}} \hat{I}_{k} \right)} \]. As the number of spin interactions between nonequivalent nuclei increase, a greater number of single quantum terms are generated.

The influence of multispin terms on the FID following RF excitation has been studied in highly polarized systems [16]. In this example, $N$ spin-$\frac{1}{2}$ nuclei are taken to be polarized along the $\hat{z}$ axis and the density matrix is defined by,

\[ \rho_{\text{sys}} = \prod_{k=1}^{N} \left( \frac{1}{2} \hat{1} + \zeta \hat{I}_k^Z \right) = \frac{1}{2^N} \hat{1} + \frac{\zeta}{2^{N-1}} \sum_{k=1}^{N} I_k^Z + \frac{\zeta^2}{2^{N-2}} \sum_{k<l} I_k^Z I_l^Z + \cdots, \]

where $I_k^Z$ is the $\hat{z}$ component of the angular momentum operator for spin $k$. For a system in thermal equilibrium, the polarization factor is given by \[ \zeta = \tanh(\alpha), \]

where $\alpha = \hbar/2k_B T$ is the ratio of Zeeman energy to thermal energy. Assuming temperature $T$ is room temperature and magnetic field strength, $B$, is "high" (around 11 Tesla, for example) then $\zeta \approx 10^{-5}$ [16]. According to the high temperature approximation, the density matrix is truncated in terms of $\rho_{\text{sys}} \approx (\hat{1} + 2\zeta \sum_k I_k^Z)/2^N$. Reducing $\rho_{\text{sys}}$ in this way excludes higher order multispin terms of $\rho_{\text{sys}}$ and neglects spin interactions responsible for evolution of these multispin terms into observable signal. When signal is detected at the probe coil [at a time $t$] only observable magnetization survive the trace condition, $S(t) \sim \text{Tr}[\hat{\rho}(t) \hat{I}^+]$. An interaction between spins is therefore necessary in order for multispin terms to evolve into observable signal. In the example of the highly polarized system, this interaction is the dipole - dipole coupling. For a standard liquid sample, such as that used in this work, the dominant coupling mechanism is spin - spin coupling.

The RIPSP generates an effective field with phase $\hat{x}$ and strength $\nu_{k,\text{RIPSP}}^\text{EFF}$ acting on the $k^{th}$ spin. When $|\nu_{k,\text{RIPSP}}^\text{EFF} - \nu_{j,\text{RIPSP}}^\text{EFF}| \gg |J_{jk}|$ for all $j$, negligible transfer of the excitation on the $k^{th}$ I spin to the other I spins occurs and when $|\nu_{k,\text{RIPSP}}^\text{EFF} - \nu_{j,\text{RIPSP}}^\text{EFF}| \leq$
$|J_{jk}|$, the excitation on the $k^{th}$ $I$ spin is transferred to the other $I$ spins. Including higher order terms in the density matrix of the system under the RIPSP propagator gives rise to the multiplet single quantum terms that are invariant to rotation under the spin-spin coupling Hamiltonian. These terms are present during acquisition and their effect is to generate line sharpening by lengthening the FID.

3.3 Materials and Methods

Samples of 98%$^{13}$C-labeled chloroform, 98%$^{13}$C-labeled dichloromethane and the three labeled sugars shown in Figure 3.1 were obtained from Cambridge Isotope Laboratories, Inc (CIL). Samples of 5% and 1%$^{13}$CHCl$_3$ and 5%$^{13}$CH$_2$Cl$_2$ were prepared in 99% CDCl$_3$ (CIL) and contained in 5 mm CDCl$_3$ susceptibility matched Shigemi tubes (Shigemi, Inc.) with sample heights of approximately 1 cm. All solutions of labeled glucose used 99% D$_2$O (Cambridge Isotope Laboratories, Inc.) as the solvent. Samples of 300 mM D-glucose with 99%$3^{13}$C [Fig. 3.1 (A)], 99%$1,2^{13}$C [Fig. 3.1 (B)], and 99%U$^{13}$C [Fig. 3.1 (C)] were prepared in D$_2$O matched Shigemi tubes. Lower concentrations of labeled sugar, 40 mM and 37 mM, D-glucose 99%$3^{13}$C were also prepared in D$_2$O matched Shigemi tubes. Samples of 300 mM and 37 mM D-glucose 99%$3^{13}$C were also evaluated in conventional 5 mm NMR tubes from Norell, Inc.

Experiments were conducted on either a 500 MHz Avance Bruker spectrometer (static magnetic field of 11.7 T and an operating frequency for $^1$H of 500.062 MHz) equipped with a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe or on a 400 MHz Avance HD Bruker spectrometer (static field strength of 9.4 T with an operating frequency of $^1$H 400.10 MHz) equipped with a 5 mm Bruker BBO probe. Each spectrum was compared against that of the 90-acquire, which served as the control spectrum for observing effects using multiple pulse programs throughout a series of experiments. The width at half height of individual peaks were calculated using Topspin on the respective spectrometer. Individual spectra and spectral regions magnified
Figure 3.1: $\alpha$ and $\beta$ anomers of $^{13}$C labeled D-glucose. [Top] 99% L-$^{13}$C, [Middle] 99% L-(1,2)-$^{13}$C and [Bottom] 99% U-$^{13}$C. All of the labeled sugars were obtained from Cambridge Isotope Laboratories, Inc.

for viewing were aligned to match a chosen peak in the 90-acquire spectrum with the scaling factors provided in the Figures when applicable. The pulse sequences used for comparison, aside from the 90-acquire on proton, were the RIPSP with and without z-filter [31][see Chp. 2], RIPSP with composite pulses, PROJECT [60] and PROJECT with z-filter [displayed in Fig. 3.2].

In Figures 3.22 and 3.20, an “imaging” sequence using a hyperbolic secant pulse [64] was applied prior to the 90-acquire and RIPSP sequence. Subtracting the spectra with and without the inversion pulse was used to determine the influence of spatial variation on field homogeneity.
Figure 3.2: The PROJECT sequence [top] produces pure $T_2$ weighted spectra by ”spin locking” the system [60]. The z-filter [45] is used to suppress unwanted zero quantum coherence that contributes to phase distortion in a spectrum. The z-filter element, outlined in red, is comprised of a frequency swept 180° pulse on the I channel applied simultaneously with the gradient on G.

3.4 Results and Discussion

Line narrowing in 5% and 1% $^{13}$C labeled chloroform [Figs. 3.3, 3.4, 3.5 and 3.6] was not significant. The RIPSP z-filter (red) and PROJECT z-filter (blue) are compared to the 90-acquire (black) for $^{13}$C labeled chloroform in Figure 3.3. The peak widths at half height calculated via Topspin were 1.257 Hz [90-acquire (black)], 1.181 Hz [RIPSP z-filter (red)] and 1.217 Hz [PROJECT z-filter (blue)]. The RIPSP composite (green), which applies a composite 90x180y90x pulse in place of the CHIRP pulse in the z-filter, is compared against 90-acquire (black) and RIPSP z-filter (red) in Figure 3.4. The RIPSP composite was slightly more narrow at half height (1.020 Hz) than the RIPSP z-filter (red). In Figure 3.5, the z-filter was removed and the RIPSP and PROJECT sequences were again compared to the 90-acquire spectrum. In
Figure 3.5 slightly greater differences were measured between the 90-acquire spectrum (black) 1.257 Hz, RIPSP (purple) 1.104 Hz and PROJECT (orange) 1.615 Hz. Upon visual inspection of Figures 3.3, 3.4 and 3.5 few differences are notable despite minor variation of the peak width measurements. A slight narrowing in the signal base of the RIPSP with composite 180° pulse [Fig.3.4].

Similarly, comparisons between the 90-acquire (black), RIPSP z-filter (red) and PROJECT z-filter spectra for 1% $^{13}$CHCl$_3$ showed no significant changes in linewidth. Values for the peak width at half height were 1.540 Hz [90-acquire (black)], 1.380 Hz [RIPSP z-filter (red)], and 1.580 Hz [PROJECT z-filter (blue)]. For $^{13}$CH$_2$Cl$_3$ [Fig. 3.7], the 90-acquire (black) and PROJECT z-filter spectra were practically the same. Unexpectedly, the RIPSP z-filter (red) was about 25% narrower than the 90-acquire. Values for the peak width at half height were 0.537 Hz [90-acquire (black)], 0.417 Hz [RIPSP z-filter (red)], and 0.545 Hz [PROJECT z-filter (blue)].

Line narrowing was not predicted for IS and $I_2S$ systems according to theory proposed in Chapter 2. Under the heteronuclear interaction, the propagator for one loop ($n_l = 1$) of the RIPSP sequence was derived using Average Hamiltonian Theory as $\hat{U}_{RIPSP,\pm} = \hat{P}_{\pm X}(\Theta_1)$; where $\Theta_1 = 16\theta \sin(2\pi J_{IS}\tau_2) \sin(2\pi J_{IS}\tau_1)$ is the effective angle of rotation under the RIPSP sequence for an IS spin system. $\hat{U}_{RIPSP,\pm}$ represents a pure spin rotation about the $\pm X$ axis. Similarly, the propagator for $I_2S$ is $\hat{U}_{RIPSP,\pm} = \hat{P}_{\pm X}(\Theta_2)$ where $\Theta_2 = 4\theta \sin(4\pi J_{IS}\tau_2) \sin(4\pi J_{IS}\tau_1)$. Under either propagator, only rotation terms are generated. For $I_nS$ spin systems with $n > 3$, multispin single and triple quantum terms are generated in addition to the rotation. However, in order for these terms to have an influence over the length of the FID, an interaction must take place between non equivalent $I$ spins.

Evaluation of more complex spin systems was carried out on three types of $^{13}$C labeled D-glucose [Fig. 3.1]. Figure 3.8 compares the spectrum of 300 mM C-3 $^{13}$C labeled D-glucose for a 90-acquire (black) the RIPSP with z-filter (red) and PROJECT with z-filter in a conventional 5 mm NMR tube. The RIPSP z-filter (red) was, on average 5.4% more narrow than the 90-acquire (black) or PROJECT z-filter
5% $^{13}$CHCl$_3$ in a Shigemi tube

Figure 3.3: A solution of 5% $^{13}$CHCl$_3$ in CDCl$_3$ was prepared by volume in a 5 mm CDCl$_3$ matched Shigemi tube. Experiments were performed on a Bruker 500 MHz Avance spectrometer with a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. Parameters for all spectra included: $N_s = 32$, $d_1 = 30$ s, acquisition time 5 s, RG = 14.4, $\omega_{RF,C}/2\pi = 11.0$ kHz and $\omega_{RF,H}/2\pi = 29.1$ kHz. $^1$H and $^{13}$C RF transmitters were set at 7.280 ppm and 77.24 ppm. Scaling factors for individual spectra are noted in the Figure. Delays for RIPSP z-filter(red) were $\tau_1 = 150\mu$s, $\tau_2 = 300\mu$s, with $n_l = 4$ and $\theta = \pi/180$. The z-filter parameters were 50 ms CHIRP pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The delay, ($\tau_2$) and loop number for PROJECT z-filter were $\tau_2 = 300\mu$s and $n_l = 29$. 
Figure 3.4: A solution of 5% $^{13}$CHCl$_3$ in CDCl$_3$ prepared by volume in a 5 mm CDCl$_3$ matched Shigemi tube. Experiments were performed on a Bruker 500 MHz Avance spectrometer with a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. Parameters for all spectra included: $N_s = 32$, $d_1 = 30$ s, acquisition time 5 s, RG = 14.4, $\omega_{RF}^C = 11.0$ kHz and $\omega_{RF}^H = 29.1$ kHz. $^1$H and $^{13}$C RF transmitters were set at 7.280 ppm and 77.24 ppm. Scaling factors for individual spectra are noted in the Figure. RIPSP composite(green) used delays $\tau_1 = 150\mu$s, $\tau_2 = 300\mu$s, with $n_l = 4$ and $\theta = \frac{7\pi}{15\mu}$.. The same parameters as those in [Fig.3.3] were used for RIPSP z-filter(red).
Figure 3.5: A solution of 5% $^{13}$CHCl$_3$ in CDCl$_3$ prepared by volume in a 5 mm CDCl$_3$ matched Shigemi tube. Experiments were performed on a Bruker 500 MHz Avance spectrometer with a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. Parameters for all spectra included: $N_s = 32$, $d_1 = 30$ s, acquisition time 5 s, $RG = 14.4$, $\frac{\omega_{het}^{13}C}{2\pi} = 11.0$ kHz and $\frac{\omega_{het}^1H}{2\pi} = 29.1$ kHz. $^1$H and $^{13}$C RF transmitters were set at 7.280 ppm and 77.24 ppm. Scaling factors for individual spectra are noted in the Figure. Delays for RIPSP (orange) were $\tau_1 = 150\mu$s, $\tau_2 = 300\mu$s, with $n_1 = 4$ and $\theta = \frac{7\pi}{180}$. The PROJECT (purple) delay was again $\tau_{n_2} = 300\mu$s and loop $n_l = 29$. 
1% $^{13}$CHCl$_3$ in a Shigemi tube

Figure 3.6: A solution of 1% $^{13}$CHCl$_3$ in CDCl$_3$ prepared by volume in a 5 mm CDCl$_3$ matched Shigemi tube. Experiments were performed on a Bruker 500 MHz Avance spectrometer with a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. Parameters for all spectra included: $N_s = 32$, $d_1 = 30$ s, acquisition time of 5 s, RG=14.4, $\frac{\omega^{13C}}{2\pi} = 11.0$ kHz, $\frac{\omega^{1H}}{2\pi} = 29.1$ kHz, and the $^1$H and $^{13}$C RF transmitters were set at 7.280 ppm and 77.24 ppm. Scaling factors for individual spectra are noted in the Figure. Delays for RIPSP z-filter(red) were $\tau_1 = 150$µs, $\tau_2 = 300$µs, with $n_l = 4$ and $\theta = \frac{\tau_2}{180}$. The z-filter parameters were 50 ms CHIRP pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The delay, ($\tau_2$) and loop number for PROJECT z-filter were $\tau_2 = 300\mu$s and $n_l = 29$. 
Figure 3.7: A solution of 5% $^{13}$CH$_2$Cl$_2$ in CDCl$_3$ was prepared by volume in a 5 mm CDCl$_3$ matched Shigemi tube. Experiments were performed on a Bruker 400 MHz AvanceHD spectrometer with a 5 mm Bruker BBO room temperature probe. Parameters for all spectra included: $N_s = 32$, $d_1 = 40$ s, acquisition time of 5 s, RG=2, $\omega_{13C}^{RF} = 11.0$ kHz, $\omega_{1H}^{RF} = 21.3$ kHz, and the $^1$H and $^{13}$C RF transmitters were set at 5.312 ppm and 53.46 ppm. Scaling factors for individual spectra are noted in the Figure. Delays for RIPSP z-filter(red) were $\tau_1 = 150 \mu$s, $\tau_2 = 300 \mu$s, with $n_l = 9$ and $\theta = \frac{7\pi}{180}$. The z-filter parameters were 50 ms CHIRP pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The delay, ($\tau_2$) and loop number for PROJECT z-filter were $\tau_2 = 300 \mu$s and $n_l = 98$. 
(blue). The 90-acquire (black) and PROJECT z-filter (blue) had nearly identical average linewidths. The signals corresponding to proton H3, those protons directly bonded to the labeled carbon, shift at 3.69 ppm for α-H3 and 3.46 ppm for β-H3. The signal for α-H2 appears at 3.52 ppm while β-H2 appears at 3.23 ppm and both α and β-H2 contribute to signal at 3.12 ppm. The α-H4 and β-H4 protons shift close to each other at 3.39 ppm and 3.38 ppm, respectively. The H6 protons for α and β glucose shift at approximately 3.76 ppm and 3.78 ppm, respectively. The most obvious line narrowing under the RIPSP z-filter is seen between 3.2 ppm and 3.5 ppm. This is the region where both α-H4 and β-H4 protons resonate as well as β-H3 and close to the resonance for α-H2 and β-H2. Additional narrowing is apparent at 3.7 ppm, which corresponds to signal from α-H3. Signal for α-H5 appears close to both H6 protons at 3.745 ppm while β-H5 appears at about 3.45 ppm. In Figure 3.9 comparison is made between the 90-acquire (black) the RIPSP with z-filter (red) and RIPSP with composite \((\frac{\pi}{2})_x - (\pi)_y - (\frac{\pi}{2})_x\) 180 pulses in place of the CHIRP pulse used in RIPSP z-filter [Fig. 3.2]. The spectrum under the RIPSP-composite (green) was as narrow as the RIPSP z-filter spectrum (red) and 5.5% more narrow than the average linewidth of the 90-acquire (black). However, compared to RIPSP z-filter, the signal from RIPSP-composite (green) was attenuated in regions except at 3.385-3.392 ppm corresponding to α and β H4 protons.

Figure 3.10 is the expanded spectrum for 300 mM C-3 \(^{13}\)C labeled D-glucose sample in a \(D_2O\) matched Shigemi tube (Shigemi, Inc). The trends for line narrowing differ slightly from those for the sample in Figure 3.8. The narrowing effect is more apparent under the RIPSP z-filter (red) with an average linewidth 12% more narrow than that of the 90-acquire. The RIPSP-composite spectrum (green), shown Figure 3.10, has the same average linewidth as the 90-acquire. Surprisingly, the PROJECT z-filter (blue), Figure 3.10, has an average linewidth 8% wider than the 90-acquire (black).

Figures 3.13, 3.14 and 3.15 compare the spectrum of 37 mM C-3 \(^{13}\)C labeled D-glucose for a 90-acquire (black) the RIPSP with z-filter (red) PROJECT with z-filter
Figure 3.8: A solution of 300 mM $L-3^{13}$C-labeled D-glucose in D$_2$O prepared in 5mm NMR tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra $N_s = 128$, $d_1 = 2$ s, acquisition time of 5 s, RG=14.3, $\nu_{13C}$ = 10.6 kHz, $\nu_{1H}$ = 30.3 kHz, and the $^1$H and $^{13}$C RF transmitters were set at 3.43 ppm and 74.13 ppm, respectively. The scaling factors, normalized to the 90 acquire shown, for individual spectra are provided in the figure. The RIPSP with z-filter included delays $\tau_1 = 150 \mu$s, $\tau_2 = 450 \mu$s, $n_l = 7$ and $\theta = \frac{7\pi}{150}$, a 50 ms CHIRP pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The PROJECT z-filter parameters were $\tau_2 = 450 \mu$s and $n_l = 58$ a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm.
Figure 3.9: A solution of 300 mM $^3$C-labeled D-glucose in D$_2$O prepared in 5mm NMR tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra, $N_s = 128$, $d_1 = 2$ s, acquisition time of 5 s, $RG=14.3$, $\frac{\omega_{13C}}{2\pi} = 10.6$ kHz, $\frac{\omega_{1H}}{2\pi} = 30.3$ kHz, and the $^1$H and $^{13}$C RF transmitters were set at 3.434 ppm and 74.13 ppm, respectively. The scaling factors, normalized to the 90 acquire shown, for individual spectra are provided in the figure. The RIPSP with z-filter included delays $\tau_1 = 150\mu$s, $\tau_2 = 450\mu$s, $n_l = 7$ and $\theta = \frac{7\pi}{180}$, a 50 ms CHIRP pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The RIPSP composite sequence used a series of $(\frac{\pi}{2})_x - (\pi)_y - (\frac{n_l\pi}{2})_x$ composite 180 pulses in place of the shaped pulse used in “RIPSP z-filter”.
Figure 3.10: A solution of 300 mM $^{13}$C-3 labeled D-glucose in D$_2$O was contained in a 5mm in D$_2$O matched Shigemi tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra $N_s = 128$, $d_1 = 2$ s, acquisition time of 5 s, RG=14.3, $\omega_{1/2}^{1/13C} = 11.2$ kHz, $\omega_{1/2}^{1H} = 30.3$ kHz, and the $^1$H and $^{13}$C RF transmitters were set at 3.41 ppm and 74.13 ppm, respectively. The scaling factors, normalized to the 90 acquire shown, for individual spectra are provided in the figure. The RIPSP with z-filter included delays $\tau_1 = 150$µs, $\tau_2 = 450$µs, $n_l = 7$ and $\theta = \frac{2\pi}{100}$, a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The PROJECT z-filter parameters were $\tau_2 = 450$µ and $n_l = 58$ a 50 ms CHIRP pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm.
Figure 3.11: A solution of 300 mM $L-3^{13}$C labeled D-glucose in D$_2$O was contained in a 5mm in D$_2$O matched Shigemi tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra $N_s = 128$, $d_1 = 2$ s, acquisition time of 5 s, RG=14.3, $\frac{\omega_{13C}}{2\pi} = 11.2$ kHz, $\frac{\omega_{1H}}{2\pi} = 30.3$ kHz, and the $^1$H and $^{13}$C RF transmitters were set at 3.41 ppm and 74.13 ppm, respectively. The scaling factors, normalized to the 90 acquire shown, for individual spectra are provided in the Figure. The RIPSP with z-filter included delays $\tau_1 = 150\mu$s, $\tau_2 = 450\mu$s, $n_l = 7$ and $\theta = \frac{7\pi}{180}$, a 50 ms CHIRP pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm.
(blue) in D₂O matched Shigemi tube. The line narrowing under the RIPSP z-filter in this example is obvious. The average linewidth for the spectrum under RIPSP z-filter (red) is 26%. The signals corresponding to proton H3 [protons directly bonded to the labeled carbon] shift at 3.69 ppm for α-H3 and 3.46 ppm for β-H3. The signal for α-H2 appears at 3.52 ppm while β-H2 appears at 3.23 ppm and both α and β-H2 contribute to signal at 3.12 ppm. α-H4 and β-H4 protons shift close to eachother at 3.39 ppm and 3.382 ppm, respectively. Comparing linewidths specifically at peak 3.382 for β-H2, we see that the RIPSP with z-filter (red) is 50% more narrow than the 90-acquire (black) and 51% more narrow than the PROJECT with z-filter (blue). The H6 protons for α and β glucose shift at approximately 3.76 ppm and 3.78 ppm, respectively. The region between 3.2 ppm and 3.5 ppm, where both α-H4 and β-H4 and β-H3 resonate, is significantly more resolved as compared to either the 90-acquire or the PROJECT z-filter. A similar resolution enhancement is apparent at 3.7 ppm for α-H3. Comparison between Matlab [49] simulations and experimental results were in agreement. Simulated spectra for D-glucose under the 90-acquire and RIPSP sequences predicted line sharpening under the RIPSP and showed no effect when the RIPSP was applied to chloroform [Fig. 3.12].

One of the conditions for generating multispin single quantum terms is interaction between nonequivalent nuclei. In considering this requisite, two additional labeled glucose molecules were studied: C1,C2-¹³C D-glucose and uniformly labeled D-glucose [Fig. 3.1]. The spectra of 300 mM C1,C2-¹³C D-glucose for a 90-acquire (black), RIPSP z-filter (red) and PROJECT with z-filter (blue) in a D₂O matched Shigemi tube is compared in [Figure 3.16]. Line narrowing by RIPSP z-filter (red) is still noticeable in this sample, but not as pronounced as in C-3 ¹³C. The fact that narrowing is still present is due to inequivalent homonuclear ¹H-¹H spin coupling. Because the protons on C1 and C2 are directly bound ¹³C, the effective field generated under the RIPSP sequence remains high compared to the heteronuclear coupling and less excitation is transfer through homonuclear ¹H-¹H coupling to the other protons. In C3 ¹³C glucose, the effective field generated by the RIPSP is less than the heteronuclear
Figure 3.12: Simulated spectra for D-glucose under the 90-acquire and RIPSP sequences predicted line sharpening under the RIPSP and showed no effect when the RIPSP was applied to chloroform.
Figure 3.13: A solution of 37 mM $^1$C-labeled glucose in D$_2$O was contained in a 5mm in D$_2$O matched Shigemi tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra $N_s = 256$, $d_1 = 2$ s, acquisition time of 5 s, $\Delta = 90.5$, $\frac{\omega_{1H}}{2\pi} = 11.4$ kHz, $\frac{\omega_{13C}}{2\pi} = 30.5$ kHz, and the $^1$H and $^{13}$C RF transmitters were set at 3.427 ppm and 74.25 ppm, respectively. The scaling factors, normalized to the 90 acquire shown, for individual spectra are provided in the figure. The RIPSP with $z$-filter included delays $\tau_1 = 150\mu$s, $\tau_2 = 450\mu$s, $n_l = 7$ and $\theta = \frac{2\pi}{15}$, a 50 ms CHIRP pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The PROJECT $z$-filter parameters were $\tau_2 = 450\mu$s and $n_l = 58$ a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm.
Figure 3.14: A solution of 37 mM $L-3^{13}\text{C}$ labeled D-glucose in D$_2$O was contained in a 5mm in D$_2$O matched Shigemi tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra $N_s = 256$, $d_1 = 2$ s, acquisition time of 5 s, RG=90.5, $\frac{\omega_{13C}}{2\pi} = 11.4$ kHz, $\frac{\omega_{1H}}{2\pi} = 30.5$ kHz, and the $^1\text{H}$ and $^{13}\text{C}$ RF transmitters were set at 3.427 ppm and 74.25 ppm, respectively. The scaling factors, normalized to the 90 acquire shown, for individual spectra are provided in the figure. The RIPSP with z-filter included delays $\tau_1 = 150$ $\mu$s, $\tau_2 = 450$ $\mu$s, $n_I = 7$ and $\theta = \frac{7\pi}{160}$, a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, $G_{\text{chirp}} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The PROJECT z-filter parameters were $\tau_2 = 450$ $\mu$s and $n_I = 58$ a 50 ms CHIRP pulse with a maximum RF amplitude of 5 kHz, $G_{\text{chirp}} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm.
Figure 3.15: A solution of 37 mM $L-3^{-13}$C labeled D-glucose in D$_2$O was contained in a 5mm in D$_2$O matched Shigemi tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra $N_s = 256$, $d_1 = 2 s$, acquisition time of 5 s, RG=90.5, $\frac{\omega_{13C}}{2\pi} = 11.4$ kHz, $\frac{\omega_{1H}}{2\pi} = 30.5$ kHz, and the $^1$H and $^{13}$C RF transmitters were set at 3.427 ppm and 74.25 ppm, respectively. The scaling factors, normalized to the 90 acquire shown, for individual spectra are provided in the figure. The RIPSP with z-filter included delays $\tau_1 = 150 \mu s$, $\tau_2 = 450 \mu s$, $n_l = 7$ and $\theta = \frac{7\pi}{180}$, a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The PROJECT z-filter parameters were $\tau_2 = 450 \mu s$ and $n_l = 58$ a 50 ms CHIRP pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm.
coupling between C3 $^{13}$C and H3, leading to a greater degree of excitation transfer to the other protons. In uniformly labeled D-glucose there is almost no apparent line narrowing, additionally, the signal under the RIPSP is significantly attenuated compared to the 90-acquire. This is due to the equivalence between protons, as all protons attached to carbons are attached to a $^{13}$C.

Spectra generated under the RIPSP z-filter sequence was compared to spectra generated under the PROJECT z-filter sequence in order to determine if the line narrowing seen in C3 labeled $^{13}$C D-glucose was result of removing fast relaxing species under the delayed acquisition time of the RIPSP. The effect of the PROJECT sequence is essentially a pulsed spin lock of transverse magnetization [60] that produces a pure $T_2$ weighted spectrum. The $T_2$ weighted spectra collected for the chloroform and methylene chloride were practically identical to the 90-acquire and RIPSP spectra. In $^{13}$C D-glucose the $T_2$ weighted spectra was always similar to the 90-acquire despite consistent line sharpening seen in the RIPSP z-filter spectra.

In order to determine if $^1$H RF inhomogeneity contributes to the spatial dependence of the RIPSP spectra, a comparison was made between the RIPSP with a z-filter comprised of the frequency swept 180$^{\text{deg}}$ pulse [Fig.3.2] and a 'z-filter' using a composite 90$^x$180$^y$90$^x$ pulse in place of the CHIRP pulse. Compared to the RIPSP with z-filter and 90-acquire, the exchange of the CHIRP pulse for the composite slightly broadened the linewidths under the RIPSP. This effect indicates that some RF inhomogeneity may be necessary to see the effect of line sharpening.

In order to determine if $^1$H RF inhomogeneity contributes to the spatial dependence of the RIPSP spectra, a comparison was made between the RIPSP with a z-filter comprised of the frequency swept 180$^{\text{deg}}$ pulse [Fig.3.2] and a 'z-filter' using a composite 90$^x$180$^y$90$^x$ pulse in place of the CHIRP pulse. Compared to the RIPSP with z-filter and 90-acquire, the exchange of the CHIRP pulse for the composite slightly broadened the linewidths under the RIPSP. This effect indicates that some RF inhomogeneity may be necessary to see the effect of line sharpening.

The requirement for a perfectly homogeneous field is one in which $n$ and $m$ equal zero and the variables $r$, $\theta$ and $\phi$ do not change. Any perturbation to the magnetic field will induce inhomogeneity. The effect of $B_0$ inhomogeneity as it pertains to shimming over a sample is examined in Figures 3.18 and 3.19. For these samples, the magnet was ”de-shimmed” to give what can be though of as ”good” bad shims, or broadened linewidth whilst retaining an overall Lorentizian or Gaussian shape. The difference in line width between the RIPSP with z-filter and 90 acquire is 15 – 20%. Qualitatively, the improvement of the RIPSP z-filter compared to the 90-acquire
Figure 3.16: A solution of 300 mM $^1$C-1,2 labeled D-glucose in D$_2$O was contained in a 5mm D$_2$O matched Shigemi tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra $N_s = 128$, $d_1 = 2$ s, acquisition time of 5 s, RG=14.3, $\frac{\nu^{13}C}{2\pi} = 10.6$ kHz, $\frac{\nu^1H}{2\pi} = 30.1$ kHz, and the $^1$H and $^{13}$C RF transmitters were set at 3.43 ppm and 83.67 ppm, respectively. The scaling factors, normalized to the 90 acquire shown, for individual spectra are provided in the figure. The RIPSP with z-filter included delays $\tau_1 = 400\mu$s, $\tau_2 = 450\mu$s, $n_l = 7$ and $\theta = \frac{\pi}{36}$, a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The PROJECT z-filter parameters were $\tau_2 = 450\mu$s and $n_l = 58$ a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm. The RIPSP composite sequence used a series of $(\frac{\pi}{2})_x - (\pi)_y - (\frac{\pi}{2})_x$ composite 180 pulses in place of the shaped pulse used in "RIPSP z-filter".
Figure 3.17: A solution of 300 mM U-13C labeled D-glucose in D2O was contained in a 5mm D2O matched Shigemi tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra $N_s = 128$, $d_1 = 2$ s, acquisition time of 5 s, $RG=14.3$, $\frac{\omega_{13C}}{2\pi} = 11.1$ kHz, $\frac{\omega_{1H}}{2\pi} = 28.9$ kHz, and the $^1H$ and $^{13}C$ RF transmitters were set at 4.15 ppm and 78.0 ppm, respectively. The scaling factor for RIPSP x-filter is provided in the figure. The RIPSP z-filter included delays $\tau_1 = 300\mu s$, $\tau_2 = 450\mu s$, $n_l = 7$ and $\theta = \frac{\pi}{36}$, a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm.
Figure 3.18: A solution of 300 mM $^1$C-3 labeled D-glucose in D$_2$O was contained in a 5mm in D$_2$O matched Shigemi tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra $N_s = 128$, $d_1 = 2$ s, acquisition time of 5 s, RG=14.3, $\frac{\Delta f_{13C}}{2\pi} = 11.1$ kHz, $\frac{\Delta f_{1H}}{2\pi} = 28.9$ kHz, and the $^1$H and $^{13}$C RF transmitters were set at 4.15 ppm and 78.0 ppm, respectively. The scaling factor for RIPSP x-filter is provided in the figure. The RIPSP z-filter included delays $\tau_1 = 300\mu$s, $\tau_2 = 450\mu$s, $n_l = 7$ and $\theta = \frac{\pi}{36}$, a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, $G_{chirp} = 1.05$ G/cm and a 1 ms crusher gradient of strength $G_{cr} = 5.2$ G/cm.
Figure 3.19: A solution of 37 mM \(L - 3^{13}C\) labeled D-glucose in D\(_2\)O was contained in a 5mm in D\(_2\)O matched Shigemi tube. Experiments were performed on a 500 MHz Avance Bruker spectrometer using a 5 mm TCI 500S2 H-C/N-D-05 Z Bruker cryoprobe. In all spectra \(N_s = 256\), \(d_1 = 2\) s, acquisition time of 5 s, \(RG=90.5\), \(\frac{\omega_{^{13}C}}{2\pi} = 11.4\) kHz, \(\frac{\omega_{^1H}}{2\pi} = 30.5\) kHz, and the \(^1H\) and \(^{13}C\) RF transmitters were set at 3.427 ppm and 74.25 ppm, respectively. The scaling factors, normalized to the 90 acquire shown, for individual spectra are provided in the figure. The RIPSP with z-filter included delays \(\tau_1 = 150\mu s\), \(\tau_2 = 450\mu s\), \(n_l = 7\) and \(\theta = \frac{\pi}{180}\), a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, \(G_{chirp} = 1.05\) G/cm and a 1 ms crusher gradient of strength \(G_{cr} = 5.2\) G/cm. The PROJECT z-filter parameters were \(\tau_2 = 450\mu s\) and \(n_l = 58\) a 50 ms chirped pulse with a maximum RF amplitude of 5 kHz, \(G_{chirp} = 1.05\) G/cm and a 1 ms crusher gradient of strength \(G_{cr} = 5.2\) G/cm.
spectra is obvious. In both concentrations of 37 mM [Fig. 3.19] and 300 mM [Fig. 3.18] multiplet structure is discernible using the RIPSP z-filter, where as the 90-acquire is not.

In Figure 3.20 the spectra were imaged using selective inversion by applying a 15 ms hyperbolic secant (HS) pulse [64] with 5 kHz bandwidth prior to the RIPSP sequence. Including a frequency modulated adiabatic inversion pulse, such as the hyperbolic secant, allows the magnetization vector $\vec{M}$ to maintain near alignment with the effective field, $\vec{B}_{\text{eff}}$. In doing so the rotation of magnetization remains invariant despite spatial inhomogeneities in the RF field, $\vec{B}_{\text{RF}}$. The spectra were subtracted with and without the inversion pulse over selections of volume of the sample. A Shigemi tube with a sample height of 1.5 cm was used for both C3 $^{13}$C D-glucose [Figs. 3.20, 3.21] and $^{13}$C methylene chloride [Fig. 3.22]. Gradients were used to select the volume over which inversion was affected. All spectra were matched in intensity for comparison. In glucose, the 90-acquire spectrum with selective inversion did not significantly change over the sample volume [Fig. 3.20]. The spectrum for selective inversion with RIPSP [Fig. 3.20] changed primarily over the region between 3.6 ppm and 3.8 ppm. Proton signals in this region correspond to 3.69 ppm for $\alpha$-H3, both H6 protons for $\alpha$ and $\beta$ glucose [3.76 ppm and 3.78 ppm], and $\alpha$-H5 at 3.745 ppm. From Figure 3.21, it is apparent that the line sharpening effect does not dramatically change over volume, however, the H6 protons do show some variation. The same set of experiments were applied to $^{13}$C methylene chloride [Fig. 3.22]. The spectra were nearly identical after being scaled to matched intensity, except for the middle 10% of the sample volume, indicating the influence of possible RF and/or $B_0$ inhomogeneity.

The z-filter uses the 180$^\circ$ frequency swept pulse to create a spin echo that refocuses zero quantum coherence [45]. The z-filter was added to the RIPSP sequence to remove the partially dispersive lineshapes that appear due to $I-I$ spin-spin coupling during the RIPSP sequence. If only pure magnetization remains following the frequency swept inversion pulse, then changing the value of the final $\theta$ pulse in Figure 3.2
Figure 3.20: Two sets of spectra were collected for selective inversion with 90-acquire or with RIPSP z-filter. The inversion pulse was an adiabatic 15 ms hyperbolic secant with a 5 kHz bandwidth added prior to the sequence. Spectra with inversion were subtracted from spectra without inversion to evaluate spatial variations in field homogeneity over the sample volume.
Figure 3.21: Two sets of spectra were collected for selective inversion with 90-acquire or with RIPSP z-filter. The inversion pulse was an adiabatic 15 ms hyperbolic secant with a 5 kHz bandwidth added prior to the sequence. Spectra with inversion was subtracted from spectra without inversion to evaluate spatial variations in field homogeneity over the sample volume.
5% $^{13}\text{CH}_2\text{Cl}_2$ in a Shigemi tube

<table>
<thead>
<tr>
<th>Without RIPSP</th>
<th>With RIPSP</th>
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<tr>
<td>% middle sample volume</td>
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Figure 3.22: Two sets of spectra were collected for selective inversion with 90-acquire or with RIPSP z-filter using a Bruker AvanceHD 400 MHz spectrometer equipped with a BBO room temperature probe. The inversion pulse was an adiabatic 15 ms hyperbolic secant with a 5 kHz bandwidth added prior to the sequence. Spectra with inversion was subtracted from spectra without inversion to evaluate spatial variations in field homogeniety over the sample volume.
should produce a spectrum that scales as $\sin \theta$. Examining Figure 3.23, variation in peak intensity is apparent for different angles of $\theta$ [Fig. 3.23]. Black arrow indicate peaks that do not scale as $(\sin \theta)$, indicating the presence of multispin terms.
Figure 3.23: Parameters for this experiment are the same as those in Figure 3.11 with the final pulse after the z-filter varied by the angle shown in the Figure. Black arrows indicate peaks which did not scale as $\sin \theta$. 
Preserving quantum coherence is of importance to a variety of fields, from quantum computing and information processing [65, 66], where unitary control of qubits is a critical requirement of many proposed algorithms, to biomedical applications, where long-lived signals can help improve resolution in imaging applications [67, 68]. As such, a variety of techniques have been developed to increase the lifetime of the coherence being studied by controlling the system-environment interactions. In dynamical decoupling [69, 70], a series of control fields are applied to the system so that, on average, the system is effectively decoupled from its environment. One common method of dynamical decoupling is the application of inversion or $\pi-$pulses to the system that are capable of preserving coherence created by an initial excitation. Examples of such dynamical decoupling sequences are the [Fig. 4.1(A)] Hahn or spin echo [71] and the [Fig. 4.1(B)] Carr-Purcell-Meiboom-Gill (CPMG) sequence [72]. These sequences refocus system-environment interactions, $\tilde{H}_{SE}$, that are odd with respect to inversion by a $\pi-$pulse applied to the system, e.g., the heteronuclear dipolar interaction between an $I$ spin (i.e., the system) and a collection of $S$ spins (i.e., the environment) [73]. The efficacy of these sequences in preserving quantum coherence, even in the presence of $\pi-$pulse errors, has been studied extensively in a variety of systems [73–77].
4.1 Background

While the $\pi-$pulses can refocus $\hat{H}_{SE}$ if it is odd under inversion by a $\pi-$pulse applied to the system, the system’s Hamiltonian, $\hat{H}_{S}$, can also be affected by the dynamical decoupling sequence. This has been shown to be the case in dipolar solids, a potential platform for quantum computing/information processing. In solids, the main spin interactions for a system of spin 1/2 nuclei are the homonuclear dipole-dipole Hamiltonian, $\hat{H}_{D}$, and the chemical shift interaction, $\hat{H}_{cs}$. In an “ideal” Hahn echo experiment [71] [Fig. 4.1(A)], $\hat{H}_{cs}$ is refocused on a time-scale of $t_1$ due to the application of a radiofrequency (RF) pulse of flip angle 180°, referred to as a $\pi-$pulse, applied at a time $\frac{t_1}{2}$. Due to the $\pi-$pulse, the system effectively evolves under $\hat{H}_{D}$ for a time $t_1$. However, additional corrections to the evolution on the order of $[\hat{H}_{D}, \hat{H}_{cs}] t_1$ contribute at large $t_1$. In order to reduce these higher-order corrections, a CPMG pulse train [72] can be used to refocus $\hat{H}_{cs}$ on a faster time scale while still enabling the system to evolve under $\hat{H}_{D}$ for long periods of time.

The CPMG$(\phi_1, \phi_2)$ pulse train consists of a series of two $\pi-$pulses with phases $\phi_1$ and $\phi_2$ and separated by a time $2\tau$ that is repeated $n_l$ times [Fig. 4.1(B)]. In Figure 4.1(B), even echoes occur at integer multiples of $4\tau$ [note that odd echoes also occur at $4n\tau + 2\tau$ for $n = 0, 1, 2, ..., but in this work, we focus on the even echoes since we are interested in studying the effects of $\pi-$pulse phases, $\phi_1$ and $\phi_2$]. In a CPMG experiment, $n_l$ echo amplitudes can be recorded in a single measurement, which is in contrast to the Hahn echo experiment, where $n_l$ different experiments are needed to record the echo amplitudes at times $t_1 = 4\tau$ to $t_1 = 4n_l\tau$. If $\hat{H}_{cs}$ is negligible or if $[\hat{H}_{cs}, \hat{H}_{D}] = 0$, then both the CPMG and the Hahn echo experiments should give identical echo amplitudes as a function of time, which are given by the free induction decay (FID) under $\hat{H}_{D}$, $\text{FID}(t) = \text{Tr} \left[ (\hat{I}_X + i\hat{I}_Y)\hat{\rho}(t) \right]$, where $\hat{I}_X$ and $\hat{I}_Y$ represent the total spin polarization along the $\hat{x}$ and $\hat{y}$ directions, respectively, and $\hat{\rho}(t)$ is the density matrix at time $t$. However, the echo amplitudes from the CPMG experiments were found [78, 79] to decay at a much slower rate than those found from the
corresponding Hahn echo experiments. Such observations are reconfirmed in Figures 4.1(C)-4.1(F), where the Hahn echoes [red, circular dots along with numerically fitted exponential decay curve (black dotted line)] are shown along with the echoes from a CPMG($Y, Y$) experiment in magnetically dilute $^{13}$C spin systems [Fig. 4.1(C)] $C_{60}$ and [Fig. 4.1(D)] $C_{70}$ and in non-dilute $^1$H systems [Fig. 4.1(E)] adamantane and [Fig. 4.1(F)] ferrocene.

There have been two main theoretical proposals to understand the long-lived spin echoes under CPMG pulse trains. One explanation, propounded by the Barrett group [80, 81], which we refer to in throughout the paper as the Barrett proposal, is that these long-lived echoes may be a consequence of resonance offset and dipolar evolution during the $\pi-$pulse, i.e., the $\pi-$pulses cannot be treated as pure $\delta$-pulses. Using average Hamiltonian theory [27] (AHT), these authors demonstrated that the CPMG($\phi_1, \phi_2$) generates an effective field that, depending on the $\pi$ pulse phases, $\phi_1$ and $\phi_2$, can spin-lock the magnetization after an initial $\left(\frac{\pi}{2}\right)\chi$ pulse; it was argued [81] that this effect was not equivalent to pulsed spin-locking. In their theory, the time $\tau$ in the CPMG pulse train was on the same order as the $\pi-$pulse time, $t_p$. The Barrett proposal was further explored in follow-up measurements which stayed in this small $\tau_c$ limit [82], suggesting that the Barrett proposal was relevant to the conditions where $\tau$ and $t_p$ are on the same order. However, it has been repeatedly shown that long-lived echoes can be generated during the CPMG experiment even when $\tau \gg t_p$, which is beyond the useful regime of the Barrett proposal [80, 81] where very complicated, higher-order terms to the average Hamiltonian would likely be needed in order to explain the CPMG experiments in this limit. An alternative theory proposed by the Levstein group [83–86], which will be referred to as the Levstein proposal in this paper, was advanced which argued that the long-lived echoes were not due to violations of the $\delta$-pulse limit but were instead the consequence of imperfect $\pi-$rotations from field inhomogeneities within the sample along with the absence of spin diffusion during the CPMG sequence. In their theory, the imperfect $\pi-$pulses could store some of the single-quantum coherence along the the direction of the large, static Zeeman
field (taken to be along the $\hat{z}$-direction) in the form of $\hat{z}$-magnetization and/or zero-quantum coherences. $\hat{z}$-magnetization or population tends to relax at a slower rate that is inversely proportional to the longitudinal relaxation time, $T_1$, relative to the relaxation decay of single-quantum coherences, which is inversely proportional to the transverse relaxation time, $T_2$. In the absence of significant spin diffusion, subsequent imperfect $\pi-$pulses could restore the zero-quantum coherences/populations back into observable single-quantum coherence to form stimulated echoes [71]. Since it is often the case in solids that $T_1 \gg T_2$, the stimulated echo would be less attenuated by relaxation than the regular spin echo generated from signal that remained single-quantum coherence throughout the $\pi-$pulse train. Levstein argued that the contributions from the stimulated echoes therefore make the echo amplitudes appear to be “artificially” long-lived. Because it was demonstrated that stimulated echoes in C$_{60}$ were present after the application of a few $\pi-$pulses [84,86], it was argued that stimulated echoes generated by magnetization coherence transfer pathways contributed at all echo times due to the periodicity of the CPMG pulse train [87,88].

In this work [89], an alternative theory for the long-lived echoes in dipolar solids observed under CPMG($\phi_1, \phi_2$) pulse trains under the conditions $\tau \gg t_p$ is considered. It is shown that form of the propagator for a CPMG($\phi_1, \phi_2$) pulse block with imperfect $\pi-$pulses (due to resonance offsets and RF flip-angle errors and neglecting $\tilde{H}_D$ during the $\pi$-pulses) is similar to the propagator for pulsed spin-locking in dipolar solids [59,90–93] with the phase of the effective “spin-locking pulses” given by $\frac{\phi_2-3\phi_1}{2}$ when $2(\phi_2 - \phi_1) = 2n\pi$ for integer $n$ (it should also be noted that previous work [73] has also suggested that spin-locking can be generated by a CPMG pulse train). Under this effective “pulsed” spin-locking generated by the CPMG pulse train, a periodic quasiequilibrium [94] that corresponds to the observed long-lived echoes under the CPMG($\phi_1, \phi_2$) pulse train can be generated only if the initial phase of the magnetization, $\phi_{init}$, is not orthogonal to the phase of the effective spin-locking field, $\phi_{init} \neq \pm (\frac{\phi_2-3\phi_1}{2} + \frac{\pi}{2})$. A reduction in the signal from the long-lived echoes along with a narrowing of the spectrum from the last echo generated by the CPMG($\phi_1, \phi_2$)
pulse train are predicted to occur as the interpulse spacing \((2\tau)\) increases; these effects were not predicted and/or observed in the previous works of the Levstein and Barrett groups. Numerical simulations along with experiments on \(C_{60}, C_{70}\), and adamantane were performed to verify these theoretical predictions.

### 4.2 Theory

Consider a system of \(N\) homonuclear, \(I = (\frac{1}{2})\) spins interacting via the dipolar interaction and placed in a strong magnetic field aligned about the \(\hat{z}\)-axis. In the high-field limit, the dipolar Hamiltonian can be written in the rotating frame of the Zeeman interaction as:

\[
\frac{\hat{H}_D}{\hbar} = \sum_{j<k} \omega_{jk}^D \left( 2\hat{I}_{Z,j}\hat{I}_{Z,k} - \hat{I}_{X,j}\hat{I}_{X,k} - \hat{I}_{Y,j}\hat{I}_{Y,k} \right)
\]

where \(\omega_{jk}^D = \frac{\gamma^2}{2} \frac{3\cos^2(\theta_{jk})-1}{r_{jk}^3}\) is the dipolar coupling constant between spins \(j\) and \(k\); \(r_{jk} = |\tilde{r}_{jk}| = |\tilde{r}_j - \tilde{r}_k|\) is the magnitude of the internuclear vector between spins \(j\) and \(k\); \(\theta_{jk} = \arccos \left( \frac{\tilde{r}_{jk} \cdot \hat{z}}{r_{jk}} \right)\) is the angle \(\tilde{r}_{jk}\) makes with the applied magnetic field. \(\hat{I}_{Z,k}, \hat{I}_{X,k},\) and \(\hat{I}_{Y,k}\) are the spin-\(\frac{1}{2}\) operators for spin \(k\). Since \([\hat{H}_D, \hat{I}_Z] = 0\), where \(\hat{I}_Z = \sum_{j=1}^{N} \hat{I}_{Z,j}\) is the total spin magnetization along the \(\hat{z}\)-direction, simultaneous orthonormal eigenstates of both \(\hat{H}_D\) and \(\hat{I}_Z\) can be found, which are denoted by \(|\epsilon_{k,n}\rangle\) where \(\hat{H}_D |\epsilon_{k,n}\rangle = \epsilon_{k,n} |\epsilon_{k,n}\rangle\), \(\hat{I}_Z |\epsilon_{k,n}\rangle = n |\epsilon_{k,n}\rangle\), and \(\langle \epsilon_{k,n}|\epsilon_{j,m}\rangle = \delta_{k,j}\delta_{m,n}\). In this case, both \(\hat{H}_D\) and \(\hat{I}_Z\) can be written in this eigenbasis as \(\hat{H}_D = \sum_{(k,n)} \epsilon_{k,n} |\epsilon_{k,n}\rangle \langle \epsilon_{k,n}|\) and \(\hat{I}_Z = \sum_{(k,n)} n |\epsilon_{k,n}\rangle \langle \epsilon_{k,n}|\). One important symmetry of \(\hat{H}_D\) is its invariance to \(\pi\)-rotations about the transverse plane, such that, \(\hat{P}_z(\pi)|\hat{H}_D|\hat{P}_z(\pi)^\dagger = \hat{H}_D\) where

\[
\hat{P}_{\theta,\phi}(\Theta) = e^{-i\Theta \left( \cos(\Theta) \hat{I}_Z + \sin(\Theta) (\hat{I}_X \cos(\phi) + \hat{I}_Y \sin(\phi)) \right)}
\]

represents a “pure” rotation of \(\Theta\) about an axis defined by spherical coordinates \((\theta, \phi)\) with \(\theta \in [0, \pi]\) and \(\phi \in [0, 2\pi]\).
Figure 4.1: (A) Hahn echo (single $\pi$-pulse) and (B) CPMG($\phi_1, \phi_2$) experiments. In a Hahn echo experiment, the echo amplitudes are collected from multiple measurements using different values of $t_1$, whereas in the CPMG($\phi_1, \phi_2$) experiment, echo amplitudes at integer multiples of $4\tau$ are collected within a single measurement. In Figs. 4.1(C)-4.1(F), the Hahn (circular red dots) and CPMG($Y, Y$) echo amplitudes (blue curve, sampled every $4\tau$) are shown for (C) $C_{60}$ [Number of scans] = 32 for the Hahn echoes; $N_s=128$ and $\tau = 500\mu s$ for the CPMG($Y, Y$) echoes], (D) $C_{70}$ [N$_s$=256 for the Hahn echoes; N$_s$=512 and $\tau = 200\mu s$ for the CPMG($Y, Y$) echoes], (E) adamantane ($C_{10}H_{16}$) [N$_s$=128 for the Hahn echoes; N$_s$=128 and $\tau = 116\mu s$ for the CPMG($Y, Y$) echoes], and (F) ferrocene ($Fe(C_5H_5)_2$) [N$_s$=128 for the Hahn echo experiment; N$_s$=256 and $\tau = 116\mu s$ for the CPMG($Y, Y$) echoes]. The echo amplitudes were normalized by the signal from a $\frac{\pi}{2}$-acquire experiment with an equivalent number of scans. In all cases, the Hahn echo amplitudes decayed at a faster rate than the corresponding CPMG($Y, Y$) echo amplitudes. Exponential fits of the Hahn echo data [$A_{exp}(-\Gamma t)$] are shown (black dotted curve) with decay constants of (C) $\Gamma = 94s^{-1}$, (D) $\Gamma = 97s^{-1}$, (E) $\Gamma = 204s^{-1}$, and (F) $\Gamma = 410s^{-1}$.
In addition to the dipolar interaction, another important interaction for \( I = 1/2 \) nuclei is the chemical shift, \( \tilde{H}_{cs} \), given by:

\[
\frac{\tilde{H}_{cs}}{\hbar} = \sum_{j=1}^{N} \omega_{cs}^{j} \hat{I}_{Z,j} = \sum_{k,m} (H_{cs})_{k,k}^{m,m} |\epsilon_{k,m}| \langle \epsilon_{k,m} | \\
+ \sum_{(k<j),m} (H_{cs})_{j,k}^{m,m} |\epsilon_{j,m}| \langle \epsilon_{k,m} | + (H_{cs})_{k,j}^{m,m} |\epsilon_{k,m}| \langle \epsilon_{j,m} | \tag{4.3}
\]

where \( (H_{cs})_{j,k}^{a,b} = \langle \epsilon_{j,a} | \frac{\tilde{H}_{cs}}{\hbar} | \epsilon_{k,b} \rangle \). In general, \( \omega_{cs}^{j} \) is anisotropic and depends upon crystallite orientation. Unlike \( \tilde{H}_{D} \), \( \tilde{H}_{cs} \) is antisymmetric with respect to \( \pi \)-rotations about the transverse plane, i.e., \( \tilde{P}_{\pi,\phi}(\pi) \tilde{H}_{cs} \tilde{P}_{\pi,\phi}^{\dagger}(\pi) = -\tilde{H}_{cs} \).

From Figure 4.1(B), the propagator for one loop of a CPMG(\( \phi_1, \phi_2 \)) pulse train \((n_l = 1)\) with perfect \( \pi \)-pulses is given by:

\[
\tilde{U}^{\text{ideal}}_{\text{CPMG},\phi_1,\phi_2}(4\tau) = \hat{U}_{f}(\tau) \hat{P}_{\phi_1,\phi_2}(\pi) \hat{U}_{f}(2\tau) \hat{P}_{\phi_1,\phi_2}(\pi) \hat{U}_{f}(\tau) \tag{4.4}
\]

where \( \hat{U}_{f}(t) = e^{-i \hat{H}_{D} + \omega_{\text{off}} \hat{I}_{Z} + \hat{H}_{cs}} \) with \( \omega_{\text{off}} \) being some global resonance offset. With perfect \( \pi \)-pulses in Equation 4.4, no long-lived echoes are predicted (as shown from simulations), and if \( \tilde{H}_{cs} = 0 \), the effects of a CPMG(\( \phi_1, \phi_2 \)) pulse train is identical to that from the corresponding Hahn echo experiments in dipolar solids. As mentioned in the introduction, previous theories for observing long-lived echoes require imperfect \( \pi \)-pulses, either through consideration of dipolar evolution during the pulse [80, 81] or due to field inhomogeneities that render the applied pulse imperfect [83–85]. While including \( \tilde{H}_{D} \) during the pulse would definitely be needed if the interpulse spacing, \( 2\tau \), was comparable to the \( \pi \)-pulse time, \( t_p = \frac{\pi}{\omega_{RF}} \) where \( \omega_{RF} \) is the strength of the applied RF field, in cases where \( 2\tau \gg t_p \) (which is the regime that was experimentally studied in this work) and where \( \tilde{H}_{D}t_p \ll 1 \), neglecting \( \tilde{H}_{D} \) during the pulse appears to not significantly alter the predictions of the following theory when \( \tau \gg t_p \). Therefore, in this work [89] the case where the \( \pi \)-pulses are “imperfect” as a result of resonance offsets during the applied pulse is considered for \( \theta \neq \frac{\pi}{2} \) in Equation 4.2 and/or for small flip-angle errors due to \( \pi \)-pulse miscalibration \( [(\omega_{RF} + \delta \omega_{RF})t_p = \Theta \neq \pi \) in Eq. (4.2)]. An “imperfect” \( \pi \)-pulse, \( \tilde{R}_{\phi}(\pi) \), can be written as:

\[
\tilde{R}_{\phi}(\pi) = e^{-it_p[(\omega_{RF}+\delta \omega_{RF})(\hat{I}_{X} \cos(\phi)+\hat{I}_{Y} \sin(\phi))+\omega_{\text{off}} \hat{I}_{Z}]} \tag{4.5}
\]
where $\delta \omega_{RF}$ and $\omega_{\text{off}}$ are due to imperfect $\pi-$pulse calibration and resonance offset, respectively. If $\left| \frac{\omega_{\text{off}}}{\omega_{RF}} \right| \ll 1$ and $\left| \frac{\delta \omega_{RF}}{\omega_{RF}} \right| \ll 1$, AHT [27] can be used to approximate $\hat{R}_{\phi}(\pi)$ in Equation 4.5 as

$$
\hat{R}_{\phi}(\pi) \approx \hat{P}_{\pi,\phi}(\pi) e^{-i \Delta H_{\text{RF}} (\hat{I}_X \cos(\phi) + \hat{I}_Y \sin(\phi)) + \frac{2 \omega_{\text{off}}}{\delta \omega}(\hat{I}_Y \cos(\phi) - \hat{I}_X \sin(\phi))}
$$

$$
= \hat{P}_{\pi,\phi}(\pi) e^{-i \frac{\delta \omega_{RF}}{\delta \omega} \hat{I}_+ e^{-i \phi} + \frac{2 \omega_{\text{off}}}{\delta \omega} \hat{T}_- e^{i \phi}}
$$

$$
= \hat{P}_{\pi,\phi}(\pi) \left[ e^{-i \frac{\delta \omega_{RF}}{\delta \omega} \sum_{(j,k,m)} \delta \omega e^{-i(\phi + \delta \phi)} (\hat{I}_+)^{m,m-1} |\epsilon_k,m\rangle \langle \epsilon_{k,m-1}|} + e^{-i \frac{\delta \omega_{RF}}{\delta \omega} \sum_{(j,k,m)} \delta \omega e^{i(\phi + \delta \phi)} (\hat{I}_-)^{m-1,m} |\epsilon_k,m\rangle \langle \epsilon_{k,m-1}|} \right]
$$

(4.6)

where $\delta \omega = \sqrt{\delta \omega_{RF}^2 + \frac{4\pi^2 \omega_{\text{off}}^2}{\delta \omega}}$, $e^{-i \delta \phi} = \frac{\delta \omega_{RF} - 2 \pi \omega_{\text{off}}}{\delta \omega}$, $\hat{I}_\pm = \hat{I}_X \pm i \hat{I}_Y$, and $(\hat{I}_\pm)_{j,k}^{a,b} = (\epsilon_j,a | \hat{I}_\pm | \epsilon_k,b)$. Note that if the pulse error is completely due to resonance offsets ($\delta \omega_{RF} = 0$), $\delta \phi = \pm \frac{\pi}{2}$, whereas if it is entirely due to flip-angle error ($\omega_{\text{off}} = 0$), $\delta \phi = 0$ or $\delta \phi = \pi$.

Analysis of CPMG($\phi_1, \phi_2$) pulse train ($n_l = 1$) using imperfect $\pi-$pulses, $\hat{R}_{\phi}(\pi)$ is considered in Equation 4.6. Under these circumstances, the propagator is given by

$$
\hat{U}_{\text{CPMG}_{\phi_1,\phi_2}}(4\tau) = \hat{U}_{\pi}(\tau) \hat{R}_{\phi_2}(\pi) \hat{U}_{\pi}(2\tau) \hat{R}_{\phi_1}(\pi) \hat{U}_{\pi}(\tau)
$$

Transforming into an interaction frame of $\hat{H}_D + \hbar \omega_{\text{off}} \hat{I}_Z$ defined by $\hat{U}(t) = e^{-i \frac{\tau}{\hbar} (\hat{H}_D + \hbar \omega_{\text{off}} \hat{I}_Z)}$, $\hat{U}_{\text{CPMG}_{\phi_1,\phi_2}}(4\tau)$ can be approximated as:

$$
\hat{U}_{\text{CPMG}_{\phi_1,\phi_2}}(4\tau) \approx \hat{P}_{0,0}(2(\phi_2 - \phi_1)) \hat{U}_D(2\tau) e^{-i \frac{2\pi}{\hbar} \hat{H}_{\text{avg}} \hat{U}_D(2\tau)}
$$

(4.7)

where $\hat{U}_D(t) = e^{-i \frac{t}{\hbar} \hat{H}_D}$ is the propagator under pure dipolar evolution, and $\hat{H}_{\text{avg}}$ is the average Hamiltonian in the interaction frame of $\hat{H}_D + \hbar \omega_{\text{off}} \hat{I}_Z$ for the CPMG($\phi_1, \phi_2$) pulse train with $n_l = 1$. The average Hamiltonian can be written as $\hat{H}_{\text{avg}} = \sum_{k=1}^{\infty} \hat{H}_{\text{avg}}^{(k)}$, where $\hat{H}_{\text{avg}}^{(k)}$ is the $k^{th}$-order contribution to $\hat{H}_{\text{avg}}$.

Contributions of $\hat{H}_{cs}$ to $\hat{H}_{\text{avg}}^{(1)}$ arise due to $[\hat{H}_D, \hat{H}_{cs}] \neq 0$, and contain only zero-quantum transitions between eigenstates of $\hat{H}_D$. These contributions of $\hat{H}_{cs}$ can be neglected during both $\tau$ and $t_p$, the first order contribution of $\hat{H}_{\text{avg}}^{(1)}$ can thus be written
in terms of spin operators as:

\[
\frac{H^{(1)}}{\hbar} = \frac{\delta \omega}{4} \left( \hat{U}_D(\tau)\hat{I}_+\hat{U}_D^\dagger(\tau)e^{-i\Delta \chi} + \hat{U}_D^\dagger(\tau)\hat{I}_-\hat{U}_D(\tau)e^{i\Delta \chi} \right) e^{i\Psi_1} \\
+ \frac{\delta \omega}{4} \left( \hat{U}_D(\tau)\hat{I}_-\hat{U}_D^\dagger(\tau)e^{i\Delta \chi} + \hat{U}_D^\dagger(\tau)\hat{I}_+\hat{U}_D(\tau)e^{-i\Delta \chi} \right) e^{-i\Psi_1} \\
= \frac{\delta \omega}{2} \hat{U}_D(\tau) \left( \hat{I}_X \cos(\Psi_1 - \Delta \chi) - \hat{I}_Y \sin(\Psi_1 - \Delta \chi) \right) \hat{U}_D^\dagger(\tau) \\
+ \frac{\delta \omega}{2} \hat{U}_D^\dagger(\tau) \left( \hat{I}_X \cos(\Psi_1 + \Delta \chi) - \hat{I}_Y \sin(\Psi_1 + \Delta \chi) \right) \hat{U}_D(\tau)
\]

(4.8)

The contributions of pulse-flip errors and offsets to \(\frac{H^{(2)}}{\hbar}\), written in terms of spin operators, again neglecting the effects of \(\tilde{H}_{es}\), is given by:

\[
\frac{H^{(2)}}{\hbar} = \frac{\delta \omega^2 t_p}{16i} \left( \hat{U}_D^\dagger(\tau)\hat{I}_+ \left( \hat{U}_D(\tau)^2 \hat{I}_+\hat{U}_D^\dagger(\tau) - \hat{U}_D^\dagger(\tau)\hat{I}_+\hat{U}_D(\tau) \right) e^{2i\Psi_1} \right) \\
+ \frac{\delta \omega^2 t_p}{16i} \left( \hat{U}_D^\dagger(\tau)\hat{I}_- \left( \hat{U}_D(\tau)^2 \hat{I}_-\hat{U}_D^\dagger(\tau) - \hat{U}_D^\dagger(\tau)\hat{I}_-\hat{U}_D(\tau) \right) e^{-2i\Psi_1} \right) \\
+ \frac{\delta \omega^2 t_p}{16i} \left( \hat{U}_D^\dagger(\tau)\hat{I}_- \left( \hat{U}_D(\tau)^2 \hat{I}_+\hat{U}_D^\dagger(\tau) - \hat{U}_D^\dagger(\tau)\hat{I}_+\hat{U}_D(\tau) \right) e^{i2\Delta \chi} \right) \\
+ \frac{\delta \omega^2 t_p}{16i} \left( \hat{U}_D^\dagger(\tau)\hat{I}_+ \left( \hat{U}_D(\tau)^2 \hat{I}_-\hat{U}_D^\dagger(\tau) - \hat{U}_D^\dagger(\tau)\hat{I}_-\hat{U}_D(\tau) \right) e^{-i2\Delta \chi} \right)
\]

(4.9)

In this case, a second-order energy shift for each state \(|\epsilon_{k,m}\rangle\) occurs along with additional zero-quantum transitions between states \(|\epsilon_{k,m}\rangle\) and \(|\epsilon_{l,m}\rangle\) and double-quantum transitions between the states \(|\epsilon_{k,m}\rangle\) and \(|\epsilon_{j,m \pm 2}\rangle\). The propagator for the CPMG(\(\phi_1, \phi_2\)) pulse block \((n_t = 1)\) in Equation 4.7 can now be rewritten more clearly:

\[
\hat{U}_{\text{CPMG}, \phi_1, \phi_2}(4\tau) \approx \hat{P}_{0,0}(2(\phi_2 - \phi_1))\hat{U}_D(2\tau)\tilde{R}_{\Psi_1}^{\text{eff}}\hat{U}_D(2\tau)
\]

(4.10)

where \(\tilde{R}_{\Psi_1}^{\text{eff}} \equiv e^{-\frac{i2\tau\Psi_1}{\hbar}}\frac{H^{(2)}}{\hbar}\) denotes an effective excitation of phase \(\Psi_1\). From Equation 4.10, the propagator under one loop \((n_t = 1)\) is equivalent to a mostly single-quantum excitation (if \(||H^{(1)}|| \gg ||H^{(2)}||\) where \(||A|| = \sqrt{\text{Tr}[A^\dagger A]}\) represents the Frobenius matrix norm) of phase \(\Psi_1\), \(\tilde{R}_{\Psi_1}^{\text{eff}}\), applied between periods of free evolution under \(\hat{H}_D\) for times \(2\tau\).

If \(\omega_{kj}^{-m-1} \tau \ll 1\) for all \((k, m)\) and \((j, m - 1)\), \(\tilde{R}_{\Psi_1}^{\text{eff}} \approx \hat{P}_{2,\Psi_1}(2\delta \omega t_p \cos(\Delta \chi))\), which can also be seen from \(\frac{H^{(1)}}{\hbar}\) in Equation 4.8 and \(\frac{H^{(2)}}{\hbar}\) in Equation 4.9 by approximating
\[ \hat{U}_D(\tau) = e^{-i\frac{\tau}{\hbar}H_D} \approx \hat{1}, \text{ then} \]

\[
\begin{align*}
\frac{H_{\text{avg}}^{(1)}}{\hbar} & = \delta \omega \cos(\Delta \chi) \left( \hat{I}_X \cos(\Psi_1) - \hat{I}_Y \sin(\Psi_1) \right) \\
\frac{H_{\text{avg}}^{(2)}}{\hbar} & = \frac{\delta \omega^2 t_p}{4} \sin(2\Delta \chi) \hat{I}_Z
\end{align*}
\]

(4.11)

In this case, \( \hat{R}^{\text{eff}}_{\Psi_1} \) is equivalent to an off resonant RF pulse of strength \( \omega^{\text{eff}}_{RF} = \delta \omega \cos(\Delta \chi) \) and phase \(-\Psi_1\), applied off-resonantly with \( \omega^{\text{eff}}_{\text{off}} = \frac{\delta \omega^2 t_p}{4} \sin(2\Delta \chi) \) for a time \( 2t_p \). However, when \( \omega_{jk}^{m,m-1} \tau \geq 1 \), \( \bar{H}_{\text{avg}} \) no longer behaves like an RF pulse and is attenuated by the transition frequencies, \( \omega_{kj}^{m,m-1} \), and by additional Bloch-Siegert [95] offset terms arising from \( \bar{H}_{\text{avg}}^{(2)} \) in Equation 4.9.

For \( n_l \) repetitions of the CPMG(\( \phi_1, \phi_2 \)) pulse block, the propagator can be rewritten as:

\[
\hat{U}_{\text{CPMG}_{\phi_1,\phi_2}}(4n_l\tau) = \hat{P}_{0,0}(2n_l(\phi_2 - \phi_1))T \prod_{k=1}^{n_l} \left( \hat{U}_D(2\tau) \hat{R}^{\text{eff}}_{\Psi_k} \hat{U}_D(2\tau) \right)
\]

(4.12)

where \( T \) is the Dyson time ordering operator, and \( \Psi_k = \Psi_1 + 2(k-1)(\phi_2 - \phi_1) \) is the effective phase of the \( k^{th} \) excitation pulse. In this work [6], analysis is restricted to the CPMG(\( X, X \)) \( \equiv \text{CPMG}(0, 0) \) \[ \Psi_1 = 0 \], CPMG(\( Y, Y \)) \( \equiv \text{CPMG}(\frac{\pi}{2}, \frac{\pi}{2}) \) \[ \Psi_1 = -\frac{\pi}{2} \], CPMG(\( X, -X \)) \( \equiv \text{CPMG}(0, \pi) \) \[ \Psi_1 = \frac{\pi}{2} \] and CPMG(\( Y, -Y \)) \( \equiv \text{CPMG}(\frac{\pi}{2}, \frac{3\pi}{2}) \) \[ \Psi_1 = 0 \] sequences, in which case, \( \hat{P}_{0,0}(2(\phi_2 - \phi_1)) = \hat{1} \) in Equation 4.12 and mod \( [\Psi_k, 2\pi] = \Psi_1 \) for all \( k \). For these CPMG sequences, the following propagators are obtained:

\[
\begin{align*}
\hat{U}_{\text{CPMG}_{Y,Y}} & = \prod_{k=1}^{n_l} \left( \hat{U}_D(2\tau) \hat{R}^{\text{eff}}_{Y} \hat{U}_D(2\tau) \right) \\
\hat{U}_{\text{CPMG}_{X,-X}} & = \prod_{k=1}^{n_l} \left( \hat{U}_D(2\tau) \hat{R}^{\text{eff}}_{Y} \hat{U}_D(2\tau) \right) \\
\hat{U}_{\text{CPMG}_{Y,-Y}} & = \prod_{k=1}^{n_l} \left( \hat{U}_D(2\tau) \hat{R}^{\text{eff}}_{X} \hat{U}_D(2\tau) \right) \\
\hat{U}_{\text{CPMG}_{X,X}} & = \prod_{k=1}^{n_l} \left( \hat{U}_D(2\tau) \hat{R}^{\text{eff}}_{X} \hat{U}_D(2\tau) \right)
\end{align*}
\]

(4.13)
Equation 4.13 represents the main theoretical result of this work [89]. The propagators in Equation 4.13 resemble a series of single-quantum excitations of either phase $\pm Y$ for the CPMG($Y, Y$) and CPMG($X, -X$) pulse trains, respectively, or of phase $X$ for the CPMG($X, X$) and CPMG($Y, -Y$) pulse trains, that are separated by a time $4\tau$ during which evolution under $\hat{H}_D$ occurs.

Before application of the CPMG pulse train, a $(\frac{\pi}{2})_X$ pulse is applied [Fig. 4.1(B)] that rotates the initial equilibrium $\hat{z}$-magnetization, $\hat{\rho}_{eq} = \hat{I}_z$, into transverse magnetization:

$$\hat{\rho}(0) = -\hat{I}_Y = \frac{i}{2} \left( \hat{I}_+ - \hat{I}_- \right) = \frac{i}{2} \sum_{(k,m) < (j,m-1)} (I_+)^{m,m-1}_{k,j} |\epsilon_{k,m}\rangle \langle \epsilon_{j,m-1}| - (I^-)^{m-1,m}_{j,k} |\epsilon_{j,m-1}\rangle \langle \epsilon_{k,m}|$$

(4.14)

The phase of the coherence between the states $|\epsilon_{k,m}\rangle$ and $|\epsilon_{j,m-1}\rangle$ in Equation 4.14 is $\phi = \frac{3\pi}{2}$, $-Y$. From Equation 4.13, both the CPMG($Y, Y$) and CPMG($X, -X$) pulse trains resemble the propagators found under pulsed spin-locking sequences of initial $\pm \hat{y}$-magnetization in dipolar solids [91–93]. It is thus predicted that the CPMG($Y, Y$) and CPMG($X, -X$) sequences can generate an effective pulsed spin-locking of initial $\hat{y}$-magnetization, whereas the CPMG($X, X$) and CPMG($Y, -Y$) sequences cannot.

While the above arguments suggest that the CPMG($Y, Y$) and CPMG($X, -X$) sequences will spin-lock those coherences with phase $\pm Y$, the strength of the spin-locking field [effective pulse] is different for the CPMG($Y, Y$) and CPMG($X, -X$) sequences and depends on the type of “error” introduced into the imperfect $\pi-$pulses, resonance offsets vs. pulse flip error. From Equation 4.15, the strength of the effective field under the CPMG($Y, Y$) pulse train for transitions that satisfy $4\omega_{j,k}^{m,m-1}\tau = 2\pi n$ for integer $n$ is proportional to $\cos \left( \frac{m\pi}{2} + \delta\phi - \omega_{off}\tau \right)$ whereas it is proportional to $\sin \left( \frac{m\pi}{2} + \delta\phi - \omega_{off}\tau \right)$ for the CPMG($X, X$) sequence. When there is only pulse flip error and $\omega_{off} = 0$, $\delta\phi = 0$ or $\delta\phi = \pi$. In this case, the effective field is nonzero for the CPMG($Y, Y$) pulse train when $n$ is even and is nonzero for the CPMG($X, -X$) pulse train when $n$ is odd. If $\omega_{off} \neq 0$, then the effective field is nonzero for both
the CPMG($Y, Y$) and CPMG($X, -X$) pulse trains, regardless of $n$. When there is only a resonance offset, such as when the pulse is applied off-resonance with $\omega_{\text{off}} \neq 0$ but with $\delta \omega_{\text{RF}} = 0$, $\delta \phi = \pm \frac{\pi}{2}$, and the spin-locking field [effective pulse] for both sequences will in general be nonzero, assuming that $\omega_{\text{off}} \tau \neq m\pi$ for integer $m$.

To illustrate the above predictions [89], numerical simulations of the CPMG sequences were performed on a “toy model” system consisting of 10 spin-1/2 particles linearly arranged along the $z$ axis, where the position of the $k^{th}$ spin was initially given by $\vec{r}_k = k\hat{z}$. The dipolar coupling constant between spins $k$ and $j$ was given by $\frac{\omega_{\text{D}}}{2\pi} = \frac{10\, \text{Hz}}{|\vec{r}_j - \vec{r}_k|}$. In order to mimic the effects of random spin distributions in solids (due to the 1% natural abundance of $^{13}$C spins) and to generate a “quasi”-continuous spectrum, the $\hat{z}$-coordinate of the $k^{th}$ spin was randomly chosen to be within the interval $[k - 0.1, k + 0.1]$ for all $k$. The dynamics under the various CPMG pulse trains were then averaged over 1250 different random configurations of the spin system, which resulted in a “quasi”-continuous spectrum with a dipolar linewidth of approximately 40 Hz. In all simulations, $\frac{\omega_{\text{RF}}}{2\pi} = 2$ kHz, and the pulses were simulated as “real” pulses, meaning that the dipolar evolution was considered during the pulse, although neglecting $\hat{H}_D$ during the pulse did not significantly affect the results of the simulations under the conditions that were studied. Thermal relaxation effects were not included in the simulations ($T_1 = T_2 = \infty$). Finally, it should be noted that an even number of spins was chosen to avoid single-quantum constants of motion [96] that are due to the invariance of $\hat{H}_D$ under $\pi$ rotations about the transverse plane.

Figure 4.2 shows a simulation of the magnitude of the echo amplitudes,

$$\left| \text{Tr} \left[ \hat{I}_+ \hat{U}_{\text{CPMG}}(t) \hat{I}_Y \hat{U}_{\text{CPMG}}^\dagger(t) \right] \right|$$

where $\hat{U}_{\text{CPMG}}(t)$ is the exact propagator under the CPMG($\phi_1, \phi_2$) sequence, evaluated at integer multiples of $4\tau$ ($\tau = 2.9$ ms) and averaged over 1250 different linear arrangements of a 10 spin system, evolving under the (black curves) CPMG($Y, Y$), (red curves) CPMG($X, -X$), (green curves) CPMG($X, X$) and (blue curves) CPMG($Y, -Y$) pulse trains. The corresponding FID from a $(\frac{\pi}{2})_X$-acquire simulation evaluated at
Figure 4.2: Numerical simulations of the (black curve) CPMG($Y, Y$), (green curve) CPMG($X, X$),
(red curve) CPMG($X, -X$), and (blue curve) CPMG($Y, -Y$) pulse trains applied to a system of
10 spins, averaged over 1250 different linear arrangements of the spins. The absolute value of
\[
\frac{\text{Tr} \left[ I_+ \hat{U}_{\text{CPMG}}(4n\tau) \hat{I}_Y \hat{U}^\dagger_{\text{CPMG}}(4n\tau) \right]}{\text{Tr} \left[ \hat{I}_Y^2 \right]} \text{ at integer multiples of } 4\tau (\tau = 2.9 \text{ ms}),
\]
where \( \hat{U}_{\text{CPMG}}(4n\tau) \) is the exact propagator for the CPMG($\phi_1, \phi_2$) sequence. The FID evaluated at integer multiples of \( 4\tau \),
\[
\frac{\text{Tr} \left[ I_+ \hat{U}_D(4n\tau) \hat{I}_Y \hat{U}^\dagger_D(4n\tau) \right]}{\text{Tr} \left[ \hat{I}_Y^2 \right]},
\]
is also shown for comparison (purple). In (A), imperfect, on resonant \( \pi \)-pulses were used in the CPMG sequences with a flip angle of \( (\omega_{\text{RF}} + \delta\omega_{\text{RF}}) t_p = \frac{9\pi}{2\pi} \) [185° pulses vs. 180° pulses]. As predicted from [Eq.4.15], only the CPMG($Y, Y$) sequence leads to any long-lived echoes (black curve) under flip-angle errors, and a clear quasiequilibrium containing nonzero \( \hat{y} \)-magnetization was observed. In (B), pulses with \( \omega_{\text{RF}} t_p = \pi \) (\( \delta\omega_{\text{RF}} = 0 \)) were applied but with a resonance offset of \( \frac{\omega_{\text{off}}}{2\pi} = 300\text{Hz} \). In this case, both the (black curve) CPMG($Y, Y$) and (red curve) CPMG($X, -X$) generated long-lived echoes. In both (A) and (B), the echo amplitudes under both the (green curve) CPMG($X, X$) and (blue curve) CPMG($Y, -Y$) pulse trains were found to decay on a time comparable to the FID from a \( \left( \frac{\pi}{2} \right)_X \)-acquire (purple curve).
integer multiples of $4\tau$, 
\[
\left[\text{purple curves, } \text{Tr}\left[ \tilde{I}_+ \tilde{U}_D(4n\tau)\tilde{I}_Y \tilde{U}_D(4n\tau) \right]\right],
\]
is shown for comparison. In Figure 4.2(A), the effect of a pulse flip error of 5$^\circ$ degrees $[(\omega_{RF} + \delta\omega_{RF})t_p = \frac{37}{30}\pi$ instead of $\omega_{RF}t_p = \pi]$ was studied, whereas in Figure 4.2(B), the pulses were applied with a resonance offset of $\frac{\omega_{RF}}{2\pi} = 300$ Hz and with $\delta\omega_{RF} = 0$. As predicted from Equation 4.13, both the (green curves) CPMG($X, X$) and (blue curves) CPMG($Y, -Y$) were unable to spin-lock the initial $\hat{y}$-magnetization generated from a $(\frac{\pi}{2})_X$ excitation pulse since the effective “pulses” generated by these sequences have phase $X$, $\hat{R}^{\text{eff}}_X$ in Equation 4.13. Therefore the echo amplitudes under the CPMG($X, X$) and CPMG($Y, Y$) pulse trains died out on a timescale comparable to the decay in the FID [purple curve] in both Figures 4.2(A) and 4.2(B). In Figure 4.2(A), the CPMG($Y, Y$) pulse train lead to long-lived echoes [black curve], whereas the CPMG($X, -X$) pulse train [red curve] did not generate any long-lived echoes. As mentioned above, this was due to the dependence of the spin-locking amplitude [Eq. 4.15] in $\overline{\mathcal{H}}^{(1)}_{\text{avg}}$ on pulse flip errors: for transitions with $\omega_{jk,m,m-1}\tau \approx 0$, $\chi_{jk,m,m-1}^m \approx 0$ and $\chi_{jk,m,m-1}^m \neq 0$ for CPMG($X, -X$) and CPMG($Y, Y$) pulse trains, respectively. This means for those transitions, the effective spin-locking field is $|\delta\omega \cos \left( \omega_{jk,m,m-1}\tau + \frac{\pi}{2} \right)| \approx |\frac{\delta\omega}{2\pi} \sin (\omega_{jk,m,m-1}\tau)| \approx 0$ Hz for the CPMG($X, -X$) pulse train and $|\frac{\delta\omega}{2\pi} \cos (\omega_{jk,m,m-1}\tau)| = 55.6$ Hz for the CPMG($Y, Y$) pulse train $[\frac{\delta\omega}{2\pi} = 55.6$ Hz in Figure 4.2(A)]. With nonzero resonance offsets, however, both the CPMG($X, -X$) [red curve, Fig. 4.2(B)] and CPMG($Y, Y$) [black curve, Fig.4.2(B)] lead to long-lived echoes due to the fact that both sequences were able to generate a nonzero spin-locking field in $\overline{\mathcal{H}}^{(1)}_{\text{avg}}$ of strength $|\frac{\delta\omega}{2\pi} \cos \left( \pi - \omega_{\text{off}}\tau \right)| = 130.7$ Hz for the CPMG($X, -X$) pulse train and $|\frac{\delta\omega}{2\pi} \cos \left( \frac{\pi}{2} - \omega_{\text{off}}\tau \right)| = 139.2$ Hz for the CPMG($Y, Y$) pulse train $[\frac{\delta\omega}{2\pi} = \frac{2\omega_{\text{off}}}{\pi} = 191$ Hz for the simulations in Fig.4.2(B)].

From the simulations in Figure 4.2, a plateau in the echo amplitudes was reached around $n_l = 20$ under the CPMG($Y, Y$)[Fig.4.2(A) and Fig.4.2(B)] and CPMG($X, -X$) [Fig. 4.2(B)] pulse trains. This plateau can be thought of as arising from a periodic quasiequilibrium [94] generated by the CPMG pulse trains that possesses a nonzero contribution corresponding to $\hat{y}$-magnetization. It has long been known [91–93] that
Figure 4.3: The effects of coherence selection during the (black curves) CPMG(Y, Y) and (red curves) CPMG(X, −X) pulse trains applied to a system of 10 spins, averaged over 200 different linear arrangements of the spins under the same conditions used in Fig. 4.2. The solid lines represent the normalized echo amplitudes without any selection (similar to the curves in Fig. 4.2), the dashed lines represent the normalized echo amplitudes where both zero- and single-quantum coherences were retained after each CPMG pulse block, and the asterisks (****) represent the normalized echo amplitudes when only single-quantum coherences were retained. As can be seen from the similarity between the echo amplitudes under no selection (solid lines) and with zero-/single-quantum coherence selection (dashed lines), the echo amplitudes are mainly governed by dynamics within the zero-quantum/single-quantum subspace.
pulsed spin-locking of magnetization in dipolar solids generates an initial quasiequilibrium state that leads to spin-locked transverse magnetization. While the $R_{q1}^{\text{eff}}$, excitation propagators in Equation 4.13 do not necessarily correspond to an RF pulse like those used in pulsed spin-locking, an analogous expression for the quasiequilibrium under the effective “pulsed” spin-locking of $\hat{\rho}(0)$ in Equation 4.14 under the CPMG propagators in Equation 4.13, $\hat{\rho}_{QE}$, can be written as:

$$\hat{\rho}_{QE} \approx \beta_{QE} \left( \frac{2t_p}{2t_p + 4\tau} \hat{H}_{\text{avg}} + \frac{4\tau}{2t_p + 4\tau} \hat{H}_D \right) = \beta_{QE} \hat{H}_{\text{eff}} \quad (4.15)$$

where $\hat{H}_{\text{eff}}$ is the average Hamiltonian under a CPMG($\phi_1, \phi_2$) pulse train ($n_t = 1$) and was derived from the propagator in Equation 4.10. The temperature, $\beta_{QE}$, is given by:

$$\beta_{QE} = \frac{\text{Tr} \left[ \hat{H}_{\text{eff}} \hat{\rho}(0) \right]}{\text{Tr} \left[ \left( \hat{H}_{\text{eff}} \right)^2 \right]} = -\frac{\text{Tr} \left[ \hat{H}_{\text{eff}} \hat{I}_Y \right]}{\text{Tr} \left[ \left( \hat{H}_{\text{eff}} \right)^2 \right]} \quad (4.16)$$

In writing Equation 4.15, the following assumptions, similar to the conditions needed under pulsed spin-locking [93], are necessary: $\hat{H}_{\text{eff}}$ is the only constant of motion for the spin system and $\tau \neq 0$, $\left| \frac{2t_p}{\hbar} \hat{H}_{\text{avg}} \right| \ll \hat{1}$ and that the spectrum of $\hat{H}_D$ lies within the range $\pm \frac{\pi}{2\tau}$. With $\hat{\rho}_{QE}$ in Equation 4.15, the fraction of transverse magnetization that is expected to be “preserved” under the CPMG($\phi_1, \phi_2$) pulse train is given by:

$$\frac{\langle \hat{I}_Y \rangle_{QE}}{\langle \hat{I}_Y(0) \rangle} = \beta_{QE} \frac{\text{Tr} \left[ \hat{I}_Y \hat{H}_{\text{eff}} \right]}{\text{Tr} \left[ \hat{I}_Y \hat{\rho}(0) \right]} = \frac{\left( \text{Tr} \left[ \hat{H}_{\text{eff}} \hat{I}_Y \right] \right)^2}{\text{Tr} \left[ \left( \hat{I}_Y \right)^2 \right] \text{Tr} \left[ \left( \hat{H}_{\text{eff}} \right)^2 \right]} \quad (4.17)$$

If $\hat{H}_{\text{avg}} \approx \hat{H}_{\text{avg}}^{(1)}$ [Eq. 4.17] can be rewritten in a compact form as:

$$\frac{\langle \hat{I}_Y \rangle_{QE}}{\langle \hat{I}_Y(0) \rangle} \approx \frac{\cos^2(\Delta \chi) \sin^2(\Psi_1) [\text{FID}_D(\tau)]^2}{1 + \cos(2\Delta \chi) \text{FID}_D(2\tau) + 4 \left( \frac{\omega_{\text{loc}}^2}{\omega_{\text{loc}}^2 + \omega_p^2} \right)^2} \quad (4.18)$$
where FID$_D(\tau)$ is the FID under pure dipolar evolution at time $\tau$:

$$\text{FID}_D(\tau) = \frac{\text{Tr} \left[ \hat{I}_Y \hat{U}_D(\tau) \hat{I}_Y \hat{U}_D^\dagger(\tau) \right]}{\text{Tr} \left[ (\hat{I}_Y)^2 \right]}$$  \hspace{1cm} (4.19)

and $\omega_{loc} = \sqrt{\frac{\text{Tr} \left[ (\hat{H}_D)^2 \right]}{\text{Tr} \left[ (\hat{I}_Y)^2 \right]}}$.

Due to the contributions of $\overline{H}^{(1)}_{\text{avg}}$ in Equation 4.8 to $\hat{\rho}_{QE}$, $\hat{y}$-magnetization will be preserved under the CPMG($Y, Y$) and CPMG($X, -X$) pulse trains since $\overline{H}^{(1)}_{\text{avg}}$ has a phase of $\Psi_1 = \pm Y$, $\sin^2(\Psi_1) = 1$, and therefore $\langle \hat{I}_Y \rangle_{QE} \neq 0$, whereas for the CPMG($X, X$) and CPMG($Y, -Y$) sequences, $\overline{H}^{(1)}_{\text{avg}}$ has a phase of $\Psi_1 = X$, $\sin^2(\Psi_1) = 0$, and therefore $\langle \hat{I}_Y \rangle_{QE} = 0$. In the simulations in Figure 4.2(A), the magnitude of the echo amplitude (for $n_l \geq 40$) relative to the initial $\hat{y}$-magnetization was $\overline{\langle \hat{I}_Y \rangle_{QE}} / \overline{\langle \hat{I}_Y(0) \rangle} = 0.1549$ under the CPMG($Y, Y$) pulse train [calculated value using Eq. 4.17 was $\overline{\langle \hat{I}_Y \rangle_{QE}} / \overline{\langle \hat{I}_Y(0) \rangle} = 0.122$], and $\overline{\langle \hat{I}_Y \rangle_{QE}} / \overline{\langle \hat{I}_Y(0) \rangle} = 0.0016$ under the CPMG($X, -X$) pulse train [calculated value using Eq. 4.17 was $\overline{\langle \hat{I}_Y \rangle_{QE}} / \overline{\langle \hat{I}_Y(0) \rangle} = 0$]. Similarly in Figure 4.2(B), the magnitude of the echo amplitude (for $n_l \geq 40$) relative to the initial $\hat{y}$-magnetization was $\overline{\langle \hat{I}_Y \rangle_{QE}} / \overline{\langle \hat{I}_Y(0) \rangle} = 0.468$ under the CPMG($Y, Y$) pulse train [calculated value using Eq. 4.17 was $\overline{\langle \hat{I}_Y \rangle_{QE}} / \overline{\langle \hat{I}_Y(0) \rangle} = 0.456$], and $\overline{\langle \hat{I}_Y \rangle_{QE}} / \overline{\langle \hat{I}_Y(0) \rangle} = 0.556$ under the CPMG($X, -X$) pulse train [calculated value using Eq. 4.17 was $\overline{\langle \hat{I}_Y \rangle_{QE}} / \overline{\langle \hat{I}_Y(0) \rangle} = 0.428$]. Possible origins for the differences between the simulated quasiequilibrium magnetization, $\overline{\langle \hat{I}_Y \rangle_{QE}} / \overline{\langle \hat{I}_Y(0) \rangle}$, and that calculated from Equation 4.17 for the 10 spin system are higher-order corrections to the average Hamiltonian treatment [93] that render the expression for $\hat{\rho}_{QE}$ in Equation 4.15 only approximate, along with other constants of motion [96] besides $\hat{H}_{\text{eff}}$.

Further numerical evidence about establishing $\hat{\rho}_{QE}$ in Equation 4.15 from initial $\hat{I}_Y$ magnetization under the CPMG($Y, Y$) and CPMG($X, -X$) pulse trains is shown in Figures 4.3. Since $\hat{\rho}_{QE}$ in Equation 4.15 is predominately made up of both single-quantum [from $\overline{H}^{(1)}_{\text{avg}}$ in Eq. 4.8] and zero-quantum terms [from $\hat{H}_D$], the majority of the spin dynamics will occur within the zero-quantum and single-quantum subspace. A justification of this assertion is shown in Figure 4.3, where the results from two
additional simulations are shown. In one of the simulations, only single-quantum coherences were retained after each CPMG pulse block [Fig. 4.3, denoted by *], and in the other simulation, both single-quantum and zero-quantum coherences were retained after each CPMG pulse block [Fig. 4.3, dashed curves]. For comparison, the simulations with no coherence selection are also shown [Fig. 4.3, solid curves]. If only single-quantum coherences were kept (asterisks in Fig. 4.3), the echo amplitudes decayed on the same time scale as the signal under a \( \frac{\pi}{2} \) \( X \) -acquire simulation [purple curves in Fig. 4.2], which is in agreement with previous numerical simulations [81] by the Barrett group. However, if both zero-quantum and single-quantum coherences were kept [dashed curves], the echo amplitudes were within 10% of the echo amplitudes when there was no coherence selection. The simulations in Figure 4.3 support the idea that the dynamics within the zero-quantum/single-quantum subspace describes establishing the quasiequilibrium, \( \hat{\rho}_{QE} \), from initial \( \hat{y} \)-magnetization.

From Equation 4.18, the echo amplitudes under the CPMG pulse trains are expected to decrease with increasing \( \tau \). This can be understood by the fact that \( \overline{H}^{(1)}_{\text{avg}} \) in Equation 4.8 looks less like an RF pulse as \( \tau \) increases, and therefore the projection of \( \overline{H}_{\text{eff}} \) onto the initial \( \hat{y} \)-magnetization decreases. However, this decrease should depend upon the dipolar transition frequency, \( \omega_{jk}^{m,m-1} \), which can be seen in the eigenstate representation of \( \overline{H}^{(1)}_{\text{avg}} \) in Equation 4.8. For those transitions that satisfy \( \omega_{jk}^{m,m-1} \tau \ll 1 \) [or in general, \( |4\omega_{jk}^{m,m-1}\tau - 2n\pi| \ll 1 \) for some integer \( n \)], \( \overline{H}^{(1)}_{\text{avg}} \) resembles an RF pulse, whereas for those transitions with \( \omega_{jk}^{m,m-1} \tau \geq 1 \), \( \overline{H}^{(1)}_{\text{avg}} \) is attenuated by the transition frequency. In this sense, coherences with a transition frequency \( \nu_{jk}^{m,m-1} \approx 0 \) Hz are expected to be spin-locked and contribute most to \( \hat{\rho}_{QE} \). A consequence of this is that the relative spectral intensity at \( \nu \approx 0 \) Hz should increase as \( \tau \) increases. This is clearly illustrated in Figure 4.4 which shows simulations of the FIDs [Fig. 4.4, left] and the corresponding spectra [Fig. 4.4, right] after the final echo under a CPMG(\( Y, Y \)) pulse train for a 10 spin system, averaged over 1250 different linear spin arrangements, under conditions of either constant excitation time \( [n_t\tau = 4.64 \text{ s}] \) in Figure 4.4(A) or constant loop number \( [n_t = 100] \) in Figure 4.4(B). In both Figure
Figure 4.4: Simulations of the (left) normalized FIDs of the final echoes and (right) corresponding spectra after application of a $\frac{\pi}{2}X-\text{CPMG}(Y, Y)$ sequence for (A) constant excitation time ($T_{tot} = 4.64$ s) and for (B) constant CPMG loop number ($n_l = 100$) in a system of 10 spins averaged over 1250 different linear arrangements of the spins. The corresponding FID and spectrum from a $\frac{\pi}{2}X$-acquire simulation are shown for comparison (black curve). In (A), simulations for constant excitation time ($T_{tot} = 4.64$ ms) are shown for the following $\tau$ and $n_l$ values: (blue curve) $\tau = 2.9$ ms and $n_l = 400$, (red curve) $\tau = 5.8$ ms and $n_l = 200$, and (green curve) $\tau = 11.6$ ms and $n_l = 100$. The resulting FIDs were attenuated relative to the signal from a $\frac{\pi}{2}X$-acquire by factors of (blue) 0.155, (red) 0.0584, and (green) 0.0265. In (B), simulations for constant loop number ($n_l = 100$) are shown for the following $\tau$ values: (blue) $\tau = 2.9$ ms, (red) $\tau = 5.8$ ms, and (green) $\tau = 11.6$ ms. In this case, the resulting FIDs were attenuated relative to the FID from a $\frac{\pi}{2}X$-acquire by factors of (blue) 0.1596, (red) 0.0587, and (green) 0.0265. In both 4.4(A) and 4.4(B), increasing $\tau$ resulted in a slower decay in the FID, leading to a sharper spectrum.
4.4(A) and 4.4(B), the FID after application of the CPMG(\(Y, Y\)) pulse train decayed more slowly with increasing \(\tau\), leading to a narrower spectrum with a larger relative intensity at \(\nu = 0\) Hz. In Figure 4.4(B), it could be argued that the narrowing of the spectra with increasing \(\tau\) was simply due to the fact that the total time of the CPMG pulse train was longer, thereby increasing the selectivity of the effective spin-locking field. However, almost identical results were obtained in the fixed excitation time simulations (\(4n_{i}\tau = 4.64\) s), where once again, the longer \(\tau\) (smaller \(n_{i}\)) simulations generated a slower decaying FID and a larger relative spectral intensity at \(\nu = 0\) Hz [Fig. 4.4(A)].

### 4.3 Materials and Methods

Experiments were performed on a 300 MHz Avance Bruker spectrometer (static magnetic field of 7 T and an operating frequency for \(^1H\) of 300.13 MHz) using a Bruker 5-mm broadband inverse (BBI) probe head at room temperature \([T=298K]\) with RF field strengths of \(\frac{\omega_{RF}}{2\pi} = 40.3\) kHz and \(\frac{\omega_{RF}}{2\pi} = 13\) kHz for \(^1H\) and \(^{13}C\), respectively.

The ferrocene (98% purity), adamantane (\(\geq 99\%\) purity), \(C_{60}\) (99.5% purity), and \(C_{70}\) (99% purity) chemicals were all purchased from Sigma-Aldrich. The adamantane and ferrocene samples were ground using a mortar and pestle before being placed in a 5mm NMR tube. In all experiments, the recycle delay times were \(d_1 = 25\) s for the adamantane and ferrocene samples, and \(d_1 = 15\) s and \(d_1 = 120\) s for the \(C_{70}\) and \(C_{60}\) samples, respectively. For the adamantane and ferrocene samples, the signals under the CPMG(\(\phi_1, \phi_2\)) and CPMG(\(-\phi_1, -\phi_2\)) pulse trains were combined in order to remove artifacts from pulse transients. In the experiments using pulsed field gradients (PFGs) on the \(C_{60}\) sample [Fig. 4.12], 300 \(\mu\)s half-sine gradient pulses were used, and a 300\(\mu\)s gradient stabilization delay was placed after the PFG and before echo acquisition. In this case, the echo acquisition time between pulses, \(T_{acq,E}\), was 800\(\mu\)s, while in all other experiments, the echo acquisition time between pulses
was given by $T_{\text{acq},E} = 2\tau - 10\mu s$. All other experimental parameters [number of scans ($N_s$), $\tau$, and $n_t$] are listed in the relevant figure captions.

4.4 Experimental Results and Theoretical Predictions

Two types of spin systems were investigated in this work [89], magnetically dilute random spin networks and non-dilute spin networks. In the case of the magnetically dilute spin systems, $^{13}$C NMR was used to study the spin dynamics under the CPMG($\phi_1, \phi_2$) pulse trains in both $C_{60}$ and $C_{70}$ ($^{13}$C has a natural abundance of around 1%). In $C_{60}$, all $^{13}$C atoms are chemically identical, and the $C_{60}$ molecule undergoes isotropic tumbling at room temperature that averages out chemical shift anisotropy and all intramolecular dipolar couplings in $C_{60}$ molecules containing more than one $^{13}$C atoms [approximately 12.1% of all $C_{60}$ molecules]. In $C_{70}$, there are five distinct $^{13}$C positions with different resonance frequencies; furthermore, $C_{70}$ does not undergo isotropic tumbling at room temperature so that both chemical shift anisotropy and intramolecular dipolar couplings are not averaged away in $C_{70}$ molecules with more than one $^{13}$C atom [around 15.5% of all $C_{70}$ molecules]. As a result, the spectral width in $C_{70}$ is much larger than that found in $C_{60}$. In $C_{60}$ and $C_{70}$, the echo amplitudes under the CPMG($Y, Y$) and CPMG($X, -X$) pulse trains were on the same order of magnitude as the signal from a $\left(\frac{\pi}{2}\right)$–acquire experiment [Fig. 4.5]. Non-dilute $^1$H spin networks in adamantane and ferrocene were also studied. Adamantane is a plastic crystal with two chemically nonequivalent $^1$H spins that undergoes isotropic molecular tumbling at room temperature, which averages away all intramolecular dipolar coupling and chemical shift anisotropy. In ferrocene, however, only one type of $^1$H spin is present, and ferrocene does not undergo isotropic tumbling at room temperature so that both chemical anisotropy and intramolecular dipolar couplings are present. In both adamantane and ferrocene, the echo amplitudes under the CPMG($Y, Y$) and CPMG($X, -X$) pulse trains were many orders of
magnitude smaller than the signal from a \( \frac{\pi}{2} \)–acquire experiment [Fig. 4.6], which was due to the relatively strong dipole-dipole couplings in these systems and the \( \tau \) values that were studied in this work, both of which result in \(|\text{FID}_D(\tau)| \ll 1\), leading to small echo amplitudes as predicted by Equation 4.18.

In Figure 4.5 and Figure 4.6, the echo amplitudes under [black curve] CPMG(\( Y, Y \)), [red curve] CPMG(\( X, -X \)), [blue curve] CPMG(\( Y, -Y \)), and [green curve] CPMG(\( X, X \)) pulse trains are shown for [Fig. 4.5] \( C_{60} \) and \( C_{70} \) and for [Fig. 4.6] adamantane and ferrocene. Although nominal \( \pi \)–pulses were applied, we estimated that the actual pulse flip errors were on the order of \( \pm (3^\circ - 4^\circ) \) for the \( ^{13}\text{C} \) experiments and \( \pm (7^\circ - 8^\circ) \) for the \( ^1\text{H} \) experiments. In all spin systems studied in this work, the CPMG(\( Y, Y \)) and CPMG(\( X, -X \)) pulse trains generated echo amplitudes that decayed more slowly than the echo amplitudes under the CPMG(\( X, X \)) and CPMG(\( Y, -Y \)) pulse trains, as predicted. Note that in the adamantane and ferrocene systems [Fig. 4.6], there was a fast initial decay of the echo amplitudes due to strong dipole-dipole coupling, which was followed by a slower decay of a small component (1\% of the initial magnetization in ferrocene and 0.1\% of the initial magnetization in adamantane).

Figure 4.7 illustrates the effects of [left] resonance offset and [right] pulse flip-angle errors on the CPMG(\( X, -X \)) and CPMG(\( Y, Y \)) pulse trains respectively in [Fig. 4.7(A)] \( C_{60} \) and [Fig. 4.7(B)] \( C_{70} \). For \( C_{60} \) [Fig. 4.7(A)], a resonance offset of \( \nu_{\text{offset}} = 2 \) kHz \([\nu_{\text{offset}}/2\pi = 13 \text{ kHz}]\) increased the echo amplitudes for the CPMG(\( X, -X \)) sequence quite dramatically [Fig. 4.7(A), left]. A similar increase in the echo amplitudes under a CPMG(\( X, -X \)) pulse train with resonance offset was seen in the simulations shown in Figure 4.2 (red curves). Furthermore, there was a slight increase in the echo amplitude when the \( \pi \)–pulses were purposefully miscalibrated (202.5\° pulse vs. a 180\° pulse), although the increase was relatively small. This indicated that the \( \pi \)–pulses were already imperfect enough to generate long-lived echoes. In \( C_{70} \) [Fig. 4.7(B)], an offset of \( \nu_{\text{offset}} = 2 \) kHz did not significantly increase the echo amplitudes [Fig. 4.7(B), left], which was likely due to the fact that there exists a large chemical shift dispersion in \( C_{70} \) due to the presence of nonequivalent \( ^{13}\text{C} \) atoms and the absence of
Figure 4.5: The echo amplitudes under the (black) CPMG(Y, Y), (red) CPMG(X, −X), (blue) CPMG(Y, −Y), and (green) CPMG(X, X) pulse trains in (A) polycrystalline C_{60} [N_s=128, \tau = 0.5 ms, and up to n_l = 400 echo amplitudes] and (B) C_{70} [N_s=384, \tau = 0.5 ms and up to n_l = 100 echo amplitudes] acquired on a 300.1 MHz Bruker spectrometer. The echo amplitudes, normalized by the signal from a \((\pi/2)_x\)–acquire experiment, are plotted at multiples of \(4\tau\). The CPMG(Y, Y) and CPMG(X, −X) pulse trains generated long-lived echoes for both [4.5(A)] C_{60} and [4.5(B)] C_{70}, whereas the CPMG(X, X) and CPMG(Y, −Y) pulse trains did not.
Figure 4.6: The echo amplitudes under the (black) CPMG(Y, Y), (red) CPMG(X, −X), (blue) CPMG(Y, −Y), and (green) CPMG(X, X) pulse trains in (A) polycrystalline adamantane \([N_s=256, \tau = 116\mu s\text{ and up to } n_l = 160 \text{ echo amplitudes}]\) and (B) ferrocene \([N_s=256, \tau = 116\mu s\text{ and up to } n_l = 160 \text{ echo amplitudes}]\) acquired on a 300.1 MHz Bruker spectrometer. The echo amplitudes, normalized by the signal from a \(\frac{\tau}{2}\)\_\(X\) \(-\)acquire experiment, are plotted at multiples of \(4\tau\). The CPMG(Y, Y) and CPMG(X, −X) pulse trains generated long-lived echoes for both [4.6(A)] adamantane and [4.6(B)] ferrocene, whereas the CPMG(X, X) and CPMG(Y, −Y) pulse trains did not.
Figure 4.7: The effects of both (right) flip-angle errors $[\omega_{RF}t_p \approx \pi$ (black curve) vs. $(\omega_{RF} + \delta\omega_{RF})t_p \approx \frac{9}{8}\pi$ (red curve)] on the echo amplitudes under a CPMG($Y, Y$) pulse train and (left) resonance offsets $[\nu_{off} = 0$ Hz (black curve) vs. $\nu_{off} = 2$ kHz (red curve)] on the echo amplitudes under a CPMG($X, -X$) pulse train in (A) polycrystalline $C_{60}$ [$N_s=128$, $\tau = 0.5$ms] and (B) $C_{70}$ [$N_s=384$ and $\tau = 0.5$ms] acquired on a 300.1 MHz Bruker spectrometer. The echo amplitudes, which were normalized by the signal from a $\pi/2$ $X$-acquire experiment, are plotted at multiples of $4\tau$. Pulse flip-angles did not have a significant effect on the echo amplitudes under the CPMG($Y, Y$) pulse trains in both $C_{60}$ and $C_{70}$ [Fig. 4.7, right], indicating that the “nominal” $\pi$–pulses were already imperfect, i.e., $\delta\omega_{RF} \neq 0$. However, resonance offsets generated larger echo amplitudes in $C_{60}$ [Fig. 4.7(A), left] under the CPMG($X, -X$) sequence due to the relatively small chemical shift dispersion in $C_{60}$, whereas offsets did not significantly affect the echo amplitudes in $C_{70}$ [Fig. 4.7(B), left] due to the already large chemical shift dispersion in $C_{70}$. 
isotropic molecular tumbling at room temperature. Again, a small increase in the echo amplitudes under a CPMG(\(Y, Y\)) pulse train was observed when using miscalibrated \(\pi\)–pulses [Fig. 4.7(B), right].

Figure 4.8 illustrates the effects of [left] resonance offset and [right] pulse flip-angle errors on the CPMG(\(X, -X\)) and CPMG(\(Y, Y\)) pulse trains, respectively, in [Fig. 4.8(A)] adamantane and [Fig. 4.8(B)] ferrocene. Application of \(\pi\)–pulses applied with a resonance offset of \(\nu_{\text{offset}} = 5\ \text{kHz}\) \(\frac{\omega_{\text{RF}}}{2\pi} = 40.3\ \text{kHz}\) lead to an increase in the echo amplitudes under a CPMG(\(X, -X\)) pulse train in both adamantane [Fig. 4.8(A), left] and ferrocene [Fig. 4.8(B), left], similar to the results in \(\text{C}_6\text{O}\) [Fig. 4.7(A), left]. This increase in the echo amplitudes was consistent with the relatively small chemical shift dispersion in both adamantane and ferrocene, which is often the case for \(^1\text{H}\) spins compared with \(^{13}\text{C}\) spins. Similar to what was seen in both \(\text{C}_6\text{O}\) and \(\text{C}_7\text{O}\) [Fig. 4.7, right], there was a slight increase in the echo amplitudes when the \(\pi\)–pulses were purposefully miscalibrated (221.5° pulses vs. 180° pulses), although the increase was relatively small. This again indicated that the \(\pi\)–pulses were already imperfect (flip-error of approximately ±7°).

The effects of a CPMG(\(Y, Y\)) pulse train on the FID and corresponding spectrum of the final echo were investigated in both [Fig. 4.9] \(\text{C}_6\text{O}\) and in [Fig. 4.10] adamantane. In both \(\text{C}_6\text{O}\) and adamantane, increasing \(\tau\) lead to a slower decay of the FID, with the largest \(\tau\) values decaying the slowest [green curves in Figs. 4.9-4.10]. This was observed under conditions of both constant total excitation time [Fig. 4.9(A) for \(\text{C}_6\text{O}\) and Fig. 4.10(A) for adamantane] and for constant loop number [Fig. 4.9(B) for \(\text{C}_6\text{O}\) and Fig. 4.10(B) for adamantane]. The CPMG(\(Y, Y\)) pulse train with the largest \(\tau\) value led to the sharpest spectra in all cases, which was similar to the simulation results in Fig. 4.4. Transitions with \(\omega_{jk}^{m,m-1}\) \(\tau \ll 1\) contribute most to the echo amplitudes under the CPMG(\(Y, Y\)) pulse trains, thus explaining the sharpening in the spectra around \(\nu \approx 0\ \text{Hz}\). One interesting note is the two resonances that appear in the adamantane spectra in Fig. 4.10. While it might be tempting to attribute the two peaks to the two different types of \(^1\text{H}\) spins in an adamantane molecule...
Figure 4.8: The effects of both (right) flip-angle errors $[\omega_{RF} t_p \approx \pi \text{ (black curve)} \text{ vs. } (\omega_{RF} + \delta\omega_{RF}) t_p \approx \frac{16}{13} \pi \text{ (red curve)}]$ on the echo amplitudes under a CPMG(Y, Y) pulse train and (left) resonance offsets $[\nu_{off} = 0 \text{ Hz (black curve)} \text{ vs. } \nu_{off} = 5 \text{ kHz (red curve)}]$ on the echo amplitudes under a CPMG(X, −X) pulse train in (A) adamantane [$N_s=256$, $\tau = 116 \mu$s] and (B) ferrocene [$N_s=256$ and $\tau = 116 \mu$s] acquired on a 300.1 MHz Bruker spectrometer. The echo amplitudes, which were normalized by the signal from a $\left(\frac{\pi}{2}\right)_X$ acquire experiment, are plotted at multiples of $4\tau$. Pulse flip-angles did not have a significant effect on the echo amplitudes under the CPMG(Y, Y) pulse trains in both adamantane and ferrocene [Fig. 4.8, right], indicating that the “nominal” $\pi$–pulses were already imperfect, i.e., $\delta\omega_{RF} \neq 0$. However, resonance offsets generated larger echo amplitudes in both adamantane [Fig. 4.8(A), left] and ferrocene [Fig. 4.8(B), left] under the CPMG(X, −X) pulse train, which was a consequence of the small chemical shift dispersion in these samples.
(similar experiments on ferrocene contained only a single peak in the spectra [data not shown]), the frequency difference between the two peaks \[\Delta \delta \approx 4.5 \text{ ppm}\] was much larger than the isotropic chemical shift difference between the two \(^1\text{H}\) spins found in solution \[\Delta \delta \approx 0.12 \text{ ppm for adamantane dissolved in deuterated chloroform}\]. The fine structure could be the result of some sort of orientation selection under the CPMG\((Y, Y)\) pulse train [97,98] or possibly a consequence of exponentially damped, sinusoidal modulations in the FID recently observed in dipolar soilds [99].

The experimental results in Figures 4.5-4.10 have all been interpreted from the view of spin thermodynamics and average Hamiltonian theory, where the CPMG\((Y, Y)\) and CPMG\((X, -X)\) pulse trains, whose propagators [Eq. (4.13)] were shown to be similar to the propagators under pulsed spin-locking of \(\hat{y}\)-magnetization, generate a quasiequilibrium with nonzero \(\hat{y}\)-magnetization. The spin dynamics under a CPMG\((\phi_1, \phi_2)\) pulse train can also be viewed in terms of coherence transfer pathways [100, 101]. It is well known that many coherence transfer pathways are generated from a CPMG pulse train with imperfect \(\pi\)-pulses. Even for a single spin-1/2, there are potentially \(3^n\) coherence transfer pathways generated from a CPMG pulse train. The periodicity of the CPMG pulse train also ensures that all possible coherence pathways that begin and end with single-quantum coherence will refocus at the time of the echo, meaning that the long-lived echoes contain contributions from all possible coherence pathways [87, 88]. As mentioned in the introduction, one proposal [83–86] for the long-lived echoes under the CPMG pulse train is that the echoes arise from stimulated echo [71] pathways. In a stimulated echo pathway, a portion of the single-quantum coherence is stored as zero-quantum coherence and/or longitudinal magnetization by an imperfect \(\pi\)-pulse, which can then be transferred back into single-quantum coherence from subsequent imperfect \(\pi\)-pulses. Due to the fact that the longitudinal relaxation time is often longer than the transverse relaxation time, \(T_1 > T_2\), pathways where the coherence is stored as longitudinal magnetization during the CPMG pulse train will, in general, decay at a slower rate than coherence pathways where the magnetization is never stored along the \(\hat{z}\)-axis.
Figure 4.9: The absolute value of the (left) FIDs for the last echo, normalized by the echo amplitude, and (right) the corresponding spectra generated from a \( \frac{\pi}{2} \)-acquire experiment under conditions of (A) constant excitation time, \( T_{\text{tot}} = 800 \) ms, and (B) constant CPMG loop number, \( n_l = 100 \), in a polycrystalline \( C_{60} \) sample acquired on a 300.1 MHz Bruker spectrometer. The FID and spectrum from a \( \frac{\pi}{2} \)-acquire experiment are shown for comparison (black curve, \( N_s = 128 \)).

(A) For the constant excitation time experiments, the following \( n_l, \tau \), and \( N_s \) values were used: (blue curve) \( \tau = 0.5 \) ms, \( n_l = 400 \) and \( N_s = 128 \), (red curve) \( \tau = 1 \) ms, \( n_l = 200 \), and \( N_s = 128 \), and (green curve) \( \tau = 2 \) ms, \( n_l = 100 \), and \( N_s = 1024 \). The corresponding echo amplitudes were attenuated (relative to the signal from a \( \frac{\pi}{2} \)-acquire experiment) by factors of (blue) 0.46, (red) 0.33, and (green) 0.15. (B) For the constant \( n_l = 100 \) experiments, the following \( \tau \) and \( N_s \) values were used: (blue) \( \tau = 0.5 \) ms with \( N_s = 128 \), (red) \( \tau = 1 \) ms with \( N_s = 256 \), and (green) \( \tau = 2 \) ms with \( N_s = 1024 \). The corresponding echo amplitudes were attenuated (relative to the signal from a \( \frac{\pi}{2} \)-acquire experiment) by factors of (blue) 0.63, (red) 0.43, and (green) 0.15. In both (A) and (B), as \( \tau \) increased, the FID decayed more slowly, resulting in a sharper spectrum.
Figure 4.10: The absolute value of (left) the FID for the last echo, normalized by the echo amplitude, and (right) the corresponding spectra generated by averaging the \( \left( \frac{\pi}{2} \right)_X - \text{CPMG}(Y, Y) \) \( n_l \) and \( \left( \frac{\pi}{2} \right)_X - \text{CPMG}(-Y, -Y) \) \( n_l \) sequences under conditions of (A) constant excitation time, \( T_{\text{tot}} = 69.24 \) ms, and (B) constant CPMG loop number, \( n_l = 60 \), in a polycrystalline adamantane sample acquired on a 300.1 MHz Bruker spectrometer. The FID from a \( \left( \frac{\pi}{2} \right)_X - \text{acquire} \) experiment and spectrum are shown for comparison (black curve, \( N_s = 128 \)). (A) For the constant excitation time experiments, the following \( n_l \), \( \tau \), and \( N_s \) values were used: (blue curve) \( \tau = 0.117 \) ms, \( n_l = 148 \), and \( N_s = 256 \); (red curve) \( \tau = 0.216 \) ms, \( n_l = 80 \), and \( N_s = 512 \); and (green curve) \( \tau = 0.321 \) ms, \( n_l = 54 \), and \( N_s = 1024 \). The corresponding echo amplitudes were attenuated (relative to the signal from a \( \left( \frac{\pi}{2} \right)_X - \text{acquire} \) experiment) by factors of (blue) \( 2.7 \times 10^{-4} \), (red) \( 1.6 \times 10^{-4} \), and (green) \( 1.2 \times 10^{-4} \). (B) For the constant \( n_l = 60 \) experiments, the following \( \tau \) and \( N_s \) values were used: (blue) \( \tau = 0.116 \) ms with \( N_s = 512 \), (red) \( \tau = 0.216 \) ms with \( N_s = 512 \), and (green) \( \tau = 0.316 \) ms with \( N_s = 1024 \). The corresponding echo amplitudes were attenuated (relative to the signal from a \( \left( \frac{\pi}{2} \right)_X - \text{acquire} \) experiment) by factors of (blue) \( 4.8 \times 10^{-4} \), (red) \( 2.0 \times 10^{-4} \), and (green) \( 1.1 \times 10^{-4} \). In both (A) and (B), as \( \tau \) increased, the FID decayed more slowly, resulting in a sharper spectrum.
In order to investigate the contributions of various coherence transfer pathways to the long-lived echoes during a CPMG(Y, Y) pulse train, the periodicity of the CPMG(Y, Y) pulse train was purposely broken by using randomly chosen delays as follows:

\[
\left(\frac{\pi}{2}\right)_X - \prod_{n=1}^{n_i} \left(\tau_n - (\pi)Y - 2\tau_n - (\pi)Y - \tau_n\right)
\]

(4.20)

where \(\tau_k \neq \tau_j\) for \(k \neq j\) but with the constraint that the total delay time, \(T_{tot} = 4 \sum_{n=1}^{n_i} \tau_n\), was the same for all experiments on a given molecule. In Figure 4.11, the FIDs (left) starting from the final echo (blue curves) along with the corresponding spectra (right) under the randomized CPMG(Y, Y) pulse train in Equation 4.20 are shown for [Fig. 4.11(A)] C\(_{60}\), [Fig. 4.11(B)] C\(_{70}\), and [Fig. 4.11(C)] adamantane. The corresponding CPMG(Y, Y) experiment using the averaged time delay, \(\langle \tau \rangle = \frac{1}{n_i} \sum_{n=1}^{n_i} \tau_n\), with \(T_{tot} = 4\langle \tau \rangle n_i\), is shown for comparison [red curves in Fig. 4.11]. In all cases, the echo amplitudes were smaller under the randomized CPMG(Y, Y) pulse train compared to the regular CPMG(Y, Y) pulse train; however, in [Fig. 4.11(B)] C\(_{70}\) and [Fig. 4.11(C)] adamantane, this reduction in echo amplitude was mainly from a decrease in the intensity from single-quantum transitions with frequencies \(\nu \neq 0\) Hz. In fact, the intensity of the resonances near \(\nu = 0\) Hz was nearly the same under both the randomized and regular CPMG(Y, Y) pulse trains in [Fig. 4.11(B)] C\(_{70}\) and [Fig. 4.11(C)] adamantane. This implies that the reduction in echo amplitude for adamantane and C\(_{70}\) under the randomized CPMG(Y, Y) pulse train was mainly a result of a line narrowing effect whereby the effective “pulsed” spin-locking field became more selective. This is consistent with previous work [102] that has demonstrated improved selectivity by “randomizing” periodic excitation sequences. In C\(_{60}\) [Fig. 4.11(A)], however, the \(\approx 74\%\) reduction in echo amplitude under the randomized CPMG(Y, Y) cannot be fully attributed to line narrowing. While there was a 27.8% reduction in the linewidth for C\(_{60}\) under the randomized CPMG sequence, the peak height at \(\nu = 0\) Hz in the spectrum was also reduced by
\[ \approx 50.5\% . \] This indicates that coherence pathways that involve changes in coherence order, such as the stimulated echo pathways, contribute to the signal at \( \nu = 0 \text{ Hz} \).

Within the context of coherence pathways, the fact that breaking the periodicity of the CPMG sequence led to increased line narrowing suggests that there is a correlation between coherence pathways and the corresponding transition frequencies, \( \omega_{kj}^{m,m-1} \). Such a correlation can be understood from the fact that single-quantum coherences with transition frequencies near \( \nu_{kj}^{m,m-1} = 0 \text{ Hz} \) and with phase \( \pm \pi \) will not change coherence order due to imperfect \( \pi \)-pulses, whereas for single-quantum coherences with transition frequencies \( |\nu_{jk}^{m,m-1}| \gg 0 \text{ Hz} \), the \( \pi \)-pulses would appear to be applied off-resonance. This argument suggests that transitions with \( |\nu_{kj}^{m,m-1}| \gg 0 \text{ Hz} \) are more likely to undergo coherence transfers due to imperfect \( \pi \)-pulses. Randomizing the CPMG pulse train prevents such coherence pathways from refocussing at the echo times, thereby resulting in a reduction in spectral intensity at transition frequencies \( |\nu_{jk}^{m,m-1}| \gg 0 \text{ Hz} \). However, the pathway picture does not provide a clear explanation for the \( \tau \) dependence of the line narrowing seen in Figures 4.9 and 4.10 and would suggest that the line narrowing should increase with \( n_l \). The opposite trend was observed in Figures 4.9(A) and 4.10(A).

Besides the coherence pathway picture, the line narrowing under the randomized CPMG pulse train in Figure 4.11 can also be understood within the context of the AHT treatment of our proposed theory. While the randomness of the delays means that an effective Hamiltonian cannot be written over the cycle of a CPMG block as was done in Equations 4.8 and 4.9, those transitions with \( \nu_{kj}^{m,m-1} \approx 0 \text{ Hz} \) will be unaffected by the random delays under \( \tilde{H}_D \) (i.e., \( \omega_{kj}^{m,m-1} \tau_k \approx 0 \) for all \( \tau_k \)), and such transitions will be effectively “pulsed” spin-locked during the course of the CPMG pulse train. This explains the observed narrowing in the spectra under the randomized CPMG\((Y, Y)\) pulse train in Figure 4.11.

Since stimulated echo pathways were considered as a potential source of the long-lived echoes [84–86] observed in \( C_{60} \), and because a reduction in spectral intensity at \( \nu \approx 0 \text{ Hz} \) under the randomized CPMG\((Y, Y)\) sequence in Figure 4.11(A) was seen
Figure 4.11: The absolute value of (left) the FIDs, which were normalized by the signal from a \( \frac{\tau}{2} \) -acquire experiment, and (right) the spectra generated from a randomized CPMG(\( Y, Y \)) pulse train in Eq. (4.20), and averaged over (A) 10 sets of random delays in C\(_{60} \) \( [T_{\text{tot}} = 0.48 \text{ s}, n_l = 100, \tau_k \in [0.4 \text{ ms}, 2 \text{ ms}] \) with \( \langle \tau \rangle = 1.2 \text{ ms} \) and \( N_s = 32 \) for each set of random delays], (B) 20 sets of random delays in C\(_{70} \) \( [T_{\text{tot}} = 58.8 \text{ ms}, n_l = 20, \tau_k \in [0.22 \text{ ms}, 1.2 \text{ ms}] \) with \( \langle \tau \rangle = 0.735 \text{ ms} \) and \( N_s = 512 \) for each set of random delays], and (C) 10 sets of random delays in adamantane \( [T_{\text{tot}} = 69.84 \text{ ms}, n_l = 90, \tau_k \in [80 \mu s, 320 \mu s] \) with \( \langle \tau \rangle = 194 \mu s \) and \( N_s = 128 \) for each set of random delays]. The corresponding constant \( \tau \) experiments (red curves) are also shown for comparison: in (A) C\(_{60} \), \( n_l = 100, \tau = 1.2 \text{ ms} \), \( T_{\text{tot}} = 4n_l\tau = 0.48 \text{ s} \), and \( N_s = 45 \), in (B) C\(_{70} \), \( n_l = 20 \tau = 0.735 \text{ ms} \), \( T_{\text{tot}} = 58.8 \text{ ms} \), and \( N_s = 2048 \), and in (C) adamantane, \( n_l = 90, \tau = 194 \mu s \), \( T_{\text{tot}} = 69.84 \text{ ms} \), and \( N_s = 512 \). The spectra were narrower from the randomized CPMG(\( Y, Y \)) compared with the spectra from the regular CPMG(\( Y, Y \)).
in this work [6], experiments were performed where CPMG(Y, Y) pulse trains that incorporated uniaxial (along the $\hat{z}$-direction) pulsed field gradients (PFGs) were applied during the delays, shown in Figure 4.12(A), in order to control the contribution from stimulated echoes to the long-lived echoes. The contribution from the stimulated pathway is attenuated by the application of half-sine shaped PFGs of length $t_g$ applied during the delays by the factor:

$$\frac{1}{z_{\text{top}} - z_{\text{bottom}}} \left| \int_{z_{\text{bottom}}}^{z_{\text{top}}} e^{i \frac{\gamma}{2} (G_j - G_k) z' t_g} dz' \right|$$

(4.21)

where the integral in Equation 4.21 extends over the sample height ($z_{\text{top}} - z_{\text{bottom}} \approx 1$ cm in our experiment). If the strengths of the PFGs are all equal ($G_1 = G_2 = G_3 = G_4$), then the stimulated echo is not attenuated, whereas if $G_1 \neq G_2 \neq G_3 \neq G_4$, the stimulated echo pathway is attenuated due to the oscillatory nature of the integrand in Equation 4.21. The use of mismatched gradients to remove stimulated echo pathways has been previously performed in early excitation sculpting experiments [103]. In Figure 4.12(B), the echo amplitudes under a CPMG(Y, Y) experiment ($\tau = 1$ ms, $n_t=100$) without PFGs (black), and with either matched PFGs [(blue) $G_1 = G_2 = G_3 = G_4 = 4.5$ G/cm, and no expected attenuation of stimulated echoes from Eq. 4.21] or mismatched PFGs [(red) $G_1 = 4.5$ G/cm, $G_2 = 3.0$ G/cm, $G_3 = 0$ G/cm, and $G_4 = 1.5$ G/cm, with a minimum attenuation of the stimulated echoes of 85.4% from Equation 4.21] are shown. Compared to the echo amplitudes in the absence of PFGs, there was a 24% and 51% reduction in echo amplitudes for the matched and mismatched PFGs, respectively [Fig. 4.12(B)]. Unlike the randomized CPMG pulse trains in Figure 4.11(A), the reduction in echo amplitude was not due to line narrowing, as can be seen from the spectra from the last echo in Figure 4.12(C), which were normalized by the echo amplitude for better comparison of the linewidths. In this case, there was no discernible difference between the normalized spectra in Figure 4.12(C), indicating that the PFGs uniformly scale the echo amplitude intensity. The fact that the echo amplitudes were reduced by 51% under mismatched gradients [Fig. 4.12(B), red] suggests that the reduction in signal at $\nu \approx 0$ Hz under the randomized CPMG(Y, Y) pulse train in Figure 4.11(A), which was $\approx 50.5\%$, comes from removing
the stimulated echo pathway in $C_{60}$. From the simulations in Figure 4.3, which indicated that the spin dynamics within the zero-quantum/single-quantum subspace was important in establishing long-lived echoes, it should also not be surprising that attenuating the contributions of the stimulated echo pathways results in a reduction in echo amplitude. With regard to the proposed theory, matched PFGs do affect $\overline{M}_{avg}$ by making $\Delta \chi$ spatially dependent, $\Delta \chi = \frac{\phi_2 - \phi_1}{2} + \delta \phi - \omega_{\text{off}} \tau - \frac{2}{\gamma} \gamma G_i z t_g$. This results in a spatial modulation of the magnitude of the pulsed “spin-locking” field, which attenuates the $\hat{y}$-magnetization component of the quasiequilibrium. For example, the maximum attenuation from matched gradients should be around 50% from Equation 4.18. For mismatched gradients, both the magnitude and direction of the the effective spin-locking field can be spatially modulated, thus reducing the quasiequilibrium magnetization even more than for the matched gradient case.
Figure 4.12: (A) Modified CPMG($Y$, $Y$) pulse train incorporating pulsed field gradients (PFGs) of strengths $G_1$, $G_2$, $G_3$ and $G_4$ before and after the $\pi-$pulses. (B) The signal from $C_{60}$ acquired during the CPMG($Y$, $Y$) sequence in Fig. 4.12(A) [$\tau = 1$ms, $n_l = 100$, and $N_s=128$] using half sine shaped, 300 $\mu$s PFGs with (blue) $G_1 = G_2 = G_3 = G_4 = 4.5$ G/cm and (red) $G_1 = 4.5$ G/cm, $G_2 = 3.0$ G/cm, $G_3 = 0$ G/cm, and $G_4 = 1.5$ G/cm. For comparison, the CPMG($Y$, $Y$) experiment without PFGs is also shown (black). With the application of PFGs, there was a 24% reduction in the echo amplitudes for (blue) the matched gradients and a 51% reduction for (red) the mismatched gradients. (C) The corresponding spectra after fourier transformation of the FID of the final echo, normalized by the corresponding echo amplitude. The linewidth of the $C_{60}$ resonance was unaffected by the PFGs.
CHAPTER 5

Conclusion

In Chapter 2, a new pathway selective pulse (PSP) based on the reverse INEPT [30] sequence was developed that can selectively excite $^1\text{H}$ spins only if they are coupled to a heteronuclear spin. While the reverse INEPT PSP or RIPSP sequence was both theoretically and experimentally shown to generate selective nutations in $I_nS$ spin systems when $2\pi J_{IS}\tau_1 \ll 1$ and $2\pi J_{IS}\tau_2 \ll 1$ (where $J_{IS}$ is the heteronuclear coupling constant), the applications of the RIPSP sequence to more complex spin systems, such as 2,3-dibromopropionic acid and brucine, resulted not only in excitation of the $^{13}\text{C}$ satellites associated with one-bond CH couplings but also in the observation of long-range $^2J_{IS}$ spin coupling. This excitation was mediated by $^1\text{H}$-$^1\text{H}$ spin-spin couplings during the RIPSP sequence and was observable due to excellent suppression of the unwanted $^1\text{H}$ signal in non $^{13}\text{C}$-containing molecules. Furthermore, the results from this work [31] indicated that the RIPSP-z-filter sequence can also generate a line narrowing of 15% – 20% in a variety of systems. In principle, the phase of the RIPSP excitation could be encoded with the $^{13}\text{C}$ chemical shift, thereby providing indirect information of the $^{13}\text{C}$ spectrum without having to perform the full 2D correlation experiment directly; a similar idea has already been utilized using polarization transfers [104]. Additionally, the RIPSP sequence could be applied as a heteronuclear spin filter or be used to study both selective spin-locking and spin diffusion in more complicated spin systems.

In Chapter 3 line sharpening under the RIPSP was treated in greater depth. While labeled chloroform and methylene chloride spectra remained relatively unchanged for
90-acquire vs. RIPSP vs PROJECT, the difference between the RIPSP z-filter vs the 90-acquire and RIPSP z-filter vs T₂ weighted spectra were significantly different for C₃¹³C labeled D-glucose. A narrowing of up to 50% was seen in 37 mM C₃¹³C D-glucose. The effect was less pronounced in C₁,C₂¹³C and non existant in uniformly labeled¹³C. This trend can be explained by the effective field generated under the RIPSP and the resulting excitation transfer which generates higher order multispin single quantum terms via nonequivalent ¹H-¹H spin coupling to those ¹H spins directly bound to¹³C. Versions of selective inversion 90-acquire and RIPSP using a frequency swept hyperbolic secant pulse were used to evaluate spatial dependence of the spins over the sample volume. Minor variations in spectra under the selective inversion indicated that RF and/or B₀ inhomogeniety are required in some capacity. The z-filter added to the RIPSP and PROJECT sequences serves to filter zero quantum coherences that contribute to dispersive line shapes. If only pure magnetization remained following the z-filter, then applying a pulse with varied θ after the z-filter should result in spectra that scales as sinθ. Variations in peak intensity following the scaling of spectra for C₃¹³C labeled D-glucose indicate that multispin terms are present upon acquisition after the z-filter. These findings lead to the conclusion that multispin terms generated by the density matrix under the RIPSP sequence leads to the lengthening of the FID and is responsible for the line sharpening seen in complex spin systems.

In Chapter 4 a general theory was presented to describe the evolution of dipolar coupled spins under a CPMG(ϕ₁,ϕ₂) pulse train using imperfect π-pulses [89]. It was demonstrated that the form of the propagator for the CPMG(Y, Y), CPMG(X, −X) pulse trains with imperfect π-pulses is similar to the propagator for pulsed spin-locking of ẑ-magnetization in dipolar solids [91–93], whereas the CPMG(X, X) and CPMG(Y, −Y) propagators can only spin-lock initial ẑ-magnetization. Similar to pulsed spin-locking in dipolar solids, we predicted that the CPMG(Y, Y),(X, −X) pulse trains could generate a periodic quasiequilibrium [94] corresponding to long-lived echoes for initial ẑ-magnetization. As the interpulse spacing (2τ) was increased,
the effective pulses under the CPMG($\phi_1, \phi_2$) pulse train became less RF-like, which led to a reduction in the signal from the long-lived echoes along with a narrowing of the resulting spectrum after the application of the CPMG pulse train. Numerical simulations along with experiments on C$_{60}$, C$_{70}$, and adamantane demonstrated this line narrowing in dipolar solids. Randomizing the delays in the CPMG pulse train also led to a reduction in echo amplitudes, although for C$_{70}$ and adamantane, this reduction was mainly due to a line narrowing in the resulting spectra with only single-quantum coherences with transition frequencies $\nu_{k,m} \approx 0$ Hz contributing to the long-lived echoes. In C$_{60}$, however, there was both a 27.8% reduction in linewidth along with a 50.5% reduction in spectral intensity at $\nu \approx 0$ Hz. Incorporating mismatched pulsed field gradients (PFGs) into the CPMG($Y, Y$) pulse train resulted in a $\approx 51\%$ reduction in intensity of the echo amplitudes in C$_{60}$, suggesting that stimulated echo pathways contribute at least 50% of the signal intensity of the long-lived echoes in C$_{60}$. The theory proposed in this work was compared to the Barrett [80, 81] and Levstein [83–86] proposals. Like both proposals, the derived theory predicts that the CPMG($Y, Y$) and CPMG($X, -X$) pulse trains can generate long-lived echoes from initial $\gamma$-magnetization while the CPMG($X, X$) and CPMG($Y, -Y$) pulse trains cannot. The theory presented in this chapter also predicts a line narrowing under the CPMG pulse trains that depends on the $\pi-$pulse spacing; such a line narrowing was not predicted and/or observed in the previous works of the Barrett and Levstein groups. Regarding the Barrett proposal, inclusion of $\mathbf{H}_D$ during the pulse does not significantly alter this theoretical result when $\tau \gg t_p$. Results for randomized CPMG and the CPMG/PFG experiments indicated that stimulated echoes contribute to 50% of the long-lived echo amplitudes in C$_{60}$.
Bibliography


[85] P. R. Levstein and M. B. Franzoni, “Comment on ”generating unexpected spin echoes in dipolar solids with pi pulses”.”


