INTRODUCTION
The implementation of two-dimensional heteronuclear correlation spectroscopy in nuclear magnetic resonance (NMR) has provided an invaluable technique for the structural analysis of large and complex molecules. In particular, for macromolecular systems containing a high number of hydrogen, carbon, and nitrogen atoms such as proteins, the combination of optimized $^{13}$C-, $^{15}$N-labeling techniques and 2D NMR has facilitated the site-specific assignments of individual amino acids and our ability to describe the connectivity in these systems.

When a collection of nuclear spins are placed in a strong magnetic field and then subjected to a slightly perturbing magnetic field induced by a radio frequency (r.f.) pulse, several types of internuclear spin couplings arise and allow for their interaction. Remarkably, given the appropriate set of experimental conditions (e.g., the r.f. power and phase, time delays, etc.), these couplings can be accessed and studied. Two types of couplings that are commonly harnessed for correlating multiple spin-$1/2$ nuclei are: (1) J-couplings, existing "through-bonds" (i.e., electrons; also referred to as scalar or indirect coupling), and (2) dipolar couplings, existing "through-space" (i.e., via dipole moments). Notably, while J couplings are frequently exploited for studying the internuclear contacts of molecules in liquid samples, this method is not as easily applied to molecular systems in the solid-state. The reason for this distinction stems from the rapid tumbling of molecules in solution, allowing for the dipolar couplings to be readily averaged to zero; however, this averaging does not occur for highly compact molecules in a rigid sample. Consequently, the additional coupling information that is collected for solid samples leads to significant spectral line broadening and decreased signal sensitivity. Accordingly, many impressive scientific efforts have been made to circumvent this challenging aspect of solid-state NMR.
SSNMR), which have culminated in part through the development of high-power proton decoupling, magic-angle spinning, and a dipolar-based coherence transfer method widely-known as cross polarization (CP).\textsuperscript{2,5}

In the paper of current focus, David Rovnyak provides a comprehensive description of the theoretical framework for cross-polarization in the context of SSNMR.\textsuperscript{5} Specifically, following an introduction to the various components of the dipolar Hamiltonian and its rotation into several different frames of reference for a simple two-spin system, an illustration of how cross-polarization from the abundant spin (\textsuperscript{1}H) to dilute spin (\textsuperscript{13}C) is achieved through a condition known as the Hartmann-Hahn matching profile. Although several additional topics are addressed in the paper (notably, the relevance of magic angle spinning in CP), this review will focus on: (1) the Hartmann-Hahn matching condition; (2) background theory for the Hamiltonian transformation; (3) the development of the heteronuclear two-spin NMR Hamiltonian; (4) a discussion of how the Hamiltonian allows for CP to proceed; and (5) the prediction of spin dynamics from the results of CP.

I. Hartmann-Hahn matching condition

The goal in applying CP to the solid sample of interest is to enhance the sensitivity of nuclei with low gyromagnetic ratios, $\gamma$, (e.g., \textsuperscript{13}C and \textsuperscript{15}N, denoted as the S spin) by enabling the transfer of magnetization initially generated on high gamma nuclei (e.g., \textsuperscript{1}H or \textsuperscript{19}F, denoted as the I spin) to the low gamma nuclei. This process is accomplished and illustrated by the pulse sequence diagram in Figure 1 (from Rovnyak Fig. 1).\textsuperscript{5}
Briefly, for a collection of nuclear spins aligned along the +z axis in the strong $B_0$ field of the NMR magnet, this sequence involves first applying a 90 degree radio frequency (r.f.) pulse (with a phase on the y-axis) to the I spin, followed by continuous r.f. irradiation on both the I and S spins to generate a dipolar coupling between them (i.e., spin-locking) and thus allow for magnetization transfer. Subsequently, the resulting signal (or free induction decay) from the low gamma nucleus is detected while simultaneously decoupling the high gamma nucleus.

Despite this rather simplified picture of CP, there are indeed many critical components that require a deeper understanding of the quantum mechanics involved to obtain high quality data. In particular, in order to achieve a coupling between the I and S spins, a certain condition known as the Hartmann-Hahn match must be met.\textsuperscript{4,5} Essentially, given that the two main types of spin-state splitting occurring in an NMR experiment are the Zeeman splitting induced by the main $B_0$ field and the splitting induced by the applied r.f. ($\propto B_1$ field), the Hartmann-Hahn matching condition takes advantage of the latter by bringing the splitting for the separate I and S spins to be equal. This $B_1$ field-induced splitting for each spin is reflected by the nutation frequency of the spin, $\omega_1$ (denoted I or S),

$$\omega_{1,I} = -\gamma_I B_{1,I} \quad \text{and} \quad \omega_{1,S} = -\gamma_S B_{1,S},$$

where $\gamma$ is the gyromagnetic ratio of the I or S nucleus. Accordingly, this matching condition can be reached by simply adjusting the power of the r.f. radiation (and thus $B_1$ field strength) being applied to each nucleus type, such that the following equation is satisfied:

$$\omega_{1,I} = \omega_{1,S} \iff \gamma_I B_{1,I} = \gamma_S B_{1,S} \quad \quad \text{[Hartmann-Hahn Match]}$$

Consequently, when this condition occurs, the energy difference between the split spin-states for each nucleus becomes the same and allows for polarization transfer to occur. (A more explicit treatment of the Hartmann-Hahn condition with respect to facilitating dipolar-based coherence transfer will be discussed shortly.)
II. Background theory for the Hamiltonian transformation

In this paper, numerous manipulations of the laboratory frame Hamiltonian are used to permit one to neglect various terms and simplify the problem. In order to understand the steps involved, however, one must explore how the Liouville-von Neumann equation can be solved using density matrices and similarity transformations. (The derivations that follow below proceed primarily from chapter 1 in Cavanagh, et al.)

It is useful to start by becoming familiar with density matrices in the Dirac notation start by expanding a ket in a chosen basis,

$$|\psi\rangle = \sum_{n=1}^{N} c_n |n\rangle,$$

and then left multiplying by $\langle m |$ so that $c_m = \langle m | \psi \rangle.$ Then,

$$|\psi\rangle = \sum_{n=1}^{N} c_n |n\rangle = \sum_{n=1}^{N} |n\rangle \langle n | \psi \rangle,$$

since $c_n$ is a scalar. One can then make use of $c_m^* = \langle \psi | m \rangle$ to write,

$$\langle \psi | H | \psi \rangle = \sum_{nm} c_m^* c_n \langle m | H | n \rangle = \sum_{nm} \langle n | \psi \rangle \langle \psi | m \rangle \langle m | H | n \rangle = \sum_n \langle n | PA | n \rangle.$$

Using the property,

$$\sum_m |m\rangle \langle m| = I \ (\text{identity}),$$

justifies the last equivalence above. And where $P = |\psi\rangle \langle \psi |$ is the density operator. Thus, $\langle \psi | H | \psi \rangle$ is equal to the trace of the matrix $\{PA\}.$

Having overviewed density matrices allows one to follow the derivation of the Liouville-von Neumann equation. Starting from the time dependent Schrödinger equation (in A.U.),

$$i \frac{d}{dt} \psi = H \psi \text{ so } \sum_n \frac{d}{dt} c_n(t) |n\rangle = -i \sum_n c_n(t) H |n\rangle,$$

left multiply through by $\langle k |$ to obtain
\[ \frac{dc_k(t)}{dt} = -i \sum_n c_n(t) \langle k|H|n \rangle. \]

Then use this relation to rewrite
\[ \frac{d\sigma(t)}{dt}, \]
by taking the derivative of the matrix of \( \sigma(t) \) with respect to time, \( t \). Doing so gives
\[ \frac{dc_k^* c_m^*}{dt} = c_k \frac{dc_m^*}{dt} + c_m \frac{dc_k^*}{dt} = i \sum_n c_k c_n^* \langle n|H|m \rangle - i \sum_n c_n c_m^* \langle k|H|n \rangle \]
as the expression for the derivative of the \( k,m \) element in the \( \sigma \) density matrix, which becomes,
\[ = i \sum_n \langle k|\sigma|n \rangle \langle n|H|m \rangle - i \sum_n \langle n|\sigma|m \rangle \langle k|H|n \rangle \]
\[ = i(\langle k|\sigma H|m \rangle - \langle k|H \sigma|m \rangle) \]

Thus, the Liouville-von Neumann equation can be written as,
\[ \frac{d\sigma(t)}{dt} = -i[H, \sigma(t)]. \]

Tackling this equation can be approached a number of different ways. Our paper makes use of the fact that if \( H \) is time independent then the solution is simply,
\[ \sigma(t) = \exp(-iHt) \sigma(0) \exp(iHt). \]

This is equivalent to having the time dependence come from phase factors for each term. However, \( H \) may or may not be time independent, so by applying the similarity transformation to give,
\[ \sigma = U \sigma_0 U^{-1}, \]
the Liouville-von Neumann equation becomes,
\[ \frac{d\sigma^T(t)}{dt} = -i[H_e, \sigma(t)], \]
where \( H_e \) is also transformed. The desire for having \( H_e \) be time-independent dictates which transformation will be used. An expression for the transformation can be obtained by,
\[ \frac{d\sigma^T(t)}{dt} = \frac{d(U \sigma(t) U^{-1})}{dt} = \frac{dU}{dt}\sigma U^{-1} + U \frac{d\sigma}{dt} U^{-1} + U\sigma \frac{dU^{-1}}{dt}. \]
\[
\frac{d\sigma^r(t)}{dt} = i[\sigma^r, UH U^{-1}] + \left[\sigma^r, \frac{dU^{-1}}{dt}\right].
\]
Writing \(U[\sigma, H]U^{-1}\) explicitly gives, \(U[\sigma, H]U^{-1} = U(\sigma H - H\sigma)U^{-1} = [\sigma^r, UHU U^{-1}]\). Then, as

\[
\frac{d\sigma^r(t)}{dt} = i[\sigma^r, UH U^{-1}] + \left[\sigma^r, \frac{dU^{-1}}{dt}\right] = i \left[\sigma^r, UHU U^{-1} - iU \frac{dU^{-1}}{dt}\right],
\]
the similarity transformation must be chosen such that,

\[
H_e = UHU^{-1} - iU \frac{dU^{-1}}{dt}.
\]

The desired transform is given in Cavanagh et al. as,

\[
U = \exp(i \omega r_{nf} J_z t),
\]
in the case that the Hamiltonian for a pulse in NMR is,

\[
H = H_x + H_{rf} = \omega_0 J_x + \omega_1[J_x \cos(\omega_{1r} t + \phi) + J_y \sin(\omega_{1r} t + \phi)],
\]
where \(H_x\) accounts for the influence of the static field and \(H_{rf}\) accounts for the r.f. pulse. Using the transform properties for, \(e^{-i\theta J_y} J_x e^{i\theta J_y}\) (where \(J_u\) and \(J_v\) are the angular momentum operators), \(H_e\) reduces to a time-independent form that can be expressed as a sum of the identity matrix and \(\sigma^z = J^- + J^+\).

III. The Heteronuclear Two-Spin NMR Hamiltonian

The full Hamiltonian used for a heteronuclear two-spin system is given in the paper as,

\[
H = H^2_I + H^2_S + H^{rf}_I + H^{rf}_S + H^D_{I1} + H^D_{I3} + H^D_{S3},
\]
where \(I\) is a highly abundant and sensitive nucleus and \(S\) is a less abundant and insensitive nucleus. The homonuclear dipole coupling terms do not exist in the heteronuclear two-spin system, but serve as a reminder of all the possible interactions that exist between nuclei in NMR. For a real system, the \(H^D_{S3}\) homonuclear dipole term can still be neglected due to the low abundance of the \(S\) nuclei; however, the \(H^D_{I1}\) term cannot be neglected.

Therefore, for the two-spin system the Hamiltonian is only,
Furthermore when $H_{IS}^P$ is expanded into several terms,

$$H_{IS}^P = \frac{\mu_0 Y_1 Y_5}{4\pi r^3} [A + B + C + D + F],$$

where each of the above components describes a different interaction between the spin angular momenta for the two nuclei in the system. However, for a heteronuclear two-spin system, only the $A$ term survives, allowing $H_{IS}^P$ to be written as,

$$H_{IS}^P = \frac{\mu_0 Y_1 Y_5}{4\pi r^3} A = \frac{\mu_0 Y_1 Y_5}{4\pi r^3} (1 - 3 \cos^2 \theta),$$

where $\theta$ is the angle between the vector connecting the two nuclei and the external magnetic field. Then, two transformations are applied simultaneously to the lab Hamiltonian, $H_{lab}$.

The first transformation changes the frame of expression for the lab Hamiltonian from the frame of the static field to that of the I and S spin r.f. frequencies,

$$H' = H_0 + H_{lab} - H_0 = H_0 + H_1,$$

where $H_0 = \omega_{rf,I} J_1^I + \omega_{rf,S} J_5^S$.

Subsequently, a transformation of the form,

$$U = \exp(iH_0 t),$$

is applied to the Hamiltonian. This is more suitable for a system with multiple nuclei of different species, though it is equivalent to the of transform provided by Cavanagh et al.

Applying the transform for $H_e$ onto $H'$ gives,

$$e^{iH_0 t} (H_0 + H_1) e^{-iH_0 t} - e^{-iH_0 t} H_0 e^{iH_0 t} = e^{iH_0 t} H_1 e^{-iH_0 t}.$$

Since $H_0$ is proportional to $J_1^I + J_5^S$, the transform yields the simplification provided in the paper as,

$$H' = e^{iH_0 t} H_1 e^{-iH_0 t},$$

by the same properties for this type of transform mentioned earlier. Thus, by that transformation (a rotation about the z axis along which the static magnetic field of the NMR instrument points), the interactions between the static field and the two spins disappear from the Hamiltonian. However, unlike in the theory section for transforming the
Hamiltonian when solving the Liouville-von Neumann equation, this transform does not remove all of the time dependence due to the presence of the coupling terms. To remove this last time dependence, integration over a time period that gives an integer number of $2\pi$ rotations is applied to average out the final time-dependent terms. To see how this results, one must look at the trigonometric forms the operator exhibits after being transformed and then time averaged—though, this algebraic exercise has been omitted for the sake of brevity. Finally, one last transformation is applied to yield,

$$H' = e^{\frac{i\pi}{2}(J_x^I + J_x^S)}H' e^{-\frac{i\pi}{2}(J_x^I + J_x^S)}.$$  

This allows the Hamiltonian to be expressed in a basis, $|I, S\rangle$, of I and S nuclear spin polarizations along the r.f. magnetic fields, instead of along the static magnetic field (e.g. $|--\rangle$ would mean that both the I and S fields are polarized as spin-up, $\alpha$).

**IV. Cross-polarization**

In light of the above derivation of the Hamiltonian and the preceding emphasis of the Hartmann-Hahn matching condition, an understanding of how cross-polarization is able to occur between two different dipole-dipole coupled nuclei may be appreciated. To more readily visualize what this dipolar-coupling entails, it is particularly revealing to analyze the matrix representation of the tilted Hamiltonian in the average rotating frame, which is given by [Rovnyak Eq. 18] $^5$:

$$H_{\text{rot}}^T = \omega_{1,I}I_Z + \omega_{1,S}S_Z + \frac{1}{2}D(I_+S_+ + I_+S_- + I_-S_+ + I_-S_-)$$

$$|++, \rangle |+-\rangle |+-\rangle |--\rangle$$

$$= \begin{bmatrix}
\frac{1}{2}(\omega_{1,I} + \omega_{1,S}) & 0 & 0 & \frac{1}{2}D \\
0 & \frac{1}{2}(\omega_{1,I} - \omega_{1,S}) & \frac{1}{2}D & 0 \\
0 & \frac{1}{2}D & \frac{1}{2}(\omega_{1,I} - \omega_{1,S}) & 0 \\
\frac{1}{2}D & 0 & 0 & \frac{1}{2}(\omega_{1,I} + \omega_{1,S})
\end{bmatrix}.$$  

In this block-diagonalized matrix, $D$ is one-half of the dipolar-coupling coefficient, $d$, as expressed by:
\[ D = \frac{1}{2} d = \frac{\gamma_1^2 \gamma_2 h}{r^3} (1 - 3 \cos^2 \theta), \]
in which \( r \) is the distance between the two nuclei (I and S) and \( \theta \) is the angle between the vector connecting both nuclei and the \( B_0 \) field (z-axis in laboratory frame).

As depicted in the Hamiltonian matrix above, each column and row indicates one of four possible spin-states that may be assumed by the heteronuclear two-spin ensemble (with the order of spins notated by, \( |IS| \)): (1) \( |+ \rangle \), both I and S spin-up; (2) \( |+ \rangle \), I spin-up, S spin-down; (3) \( |- \rangle \), I spin-down, S spin-up; and (4) \( |- \rangle \) both spin-down. Furthermore, it is useful to recognize the diagonal elements as representing the population density of each state, while the off-diagonal elements represent coherences that exist between the corresponding states.

Provided this matrix representation, it may also be noticed that there appear to be two independent types of spin state transitions, or subspaces—a double quantum (DQ) subspace (identified under the \( |+ \rangle \) and \( |- \rangle \) states) and a zero quantum (ZQ) subspace (identified under the \( |+ \rangle \) and \( |- \rangle \) states). The transition that occurs in the DQ subspace can be depicted as both the I and S spins changing in the same direction (i.e., both \( +\frac{1}{2} \) to \( -\frac{1}{2} \), and vice-versa; also known as a "flip-flip" or "flop-flop" transitions), while in the ZQ space the I and S spins change in the opposite direction to opposing states (i.e., I \( +\frac{1}{2} \) and S \( -\frac{1}{2} \) to I \( -\frac{1}{2} \) and S \( +\frac{1}{2} \), and vice-versa; also known as "flip-flop" transitions).

Now, upon taking the Hartmann-Hahn matching condition into account and assuming that,
\[ \omega_{1,I} = \omega_{1,S}, \]
the interesting effect that this would have on the Hamiltonian can be easily seen—specifically, the diagonal elements for the ZQ transition states reduce to zero, leaving only the off-diagonal elements for coherence exchange. As a direct result, the populations of the \( |+ \rangle \) and \( |- \rangle \) states is driven toward a coherence mixing of the two. Moreover, the occurrence of DQ transitions may also be observed, as the dipolar coupling terms still remain in the Hamiltonian. Indeed, these can be recorded and analyzed in experiment as
well; however, depending on the type of information that one may be interested in collecting or the experiment that one may perform, it is possible to filter out either DQ or ZQ coherences.

V. Prediction of spin dynamics
To review what has been discussed so far, we have provided a general background and description of how to arrive at the Hamiltonian for a heteronuclear two-spin system: (1) begin with the Hamiltonian in the lab frame of reference, (2) rotate this Hamiltonian into the average double rotating frame, (3) transform this Hamiltonian into the tilted frame, and finally (4) obtaining a diagonalized form of the tilted Hamiltonian in the double rotating frame, containing both ZQ and DQ subspaces. Accordingly, what follows from this step is the complete prediction of the spin dynamics for the two-spin system over time. Although the details of this density operator propagation will not be covered in this review, it is nonetheless valuable to briefly return to the significance of the initial derivation of the Liouville-von Neumann equation that was performed earlier. In particular, in order to observe what happens to the system over a period of time, the Liouville-von Neumann equation is evaluated for the Hamiltonian at a designated point in time, $t$. After doing this, the resulting Hamiltonian must then transformed back out of the diagonalized form and then returned to the laboratory frame (or double rotating and tilted frame), followed by the operation of the $S_r$ to measure the signal generated on the S spin.$^5$

REFERENCES

CONTRIBUTIONS
Dennis Piehl – Introduction, Sections I, IV, V
Daniel Torres – Sections II, III
Both – Discussions of each section1