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Three pulse recoupling and phase jump matching

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Abstract

The paper describes a family of novel recoupling pulse sequences, called three pulse recoupling. These pulse sequences can be employed for both homonuclear and heteronuclear recoupling experiments and are robust to dispersion in chemical shifts and rf-inhomogeneity. These recoupling pulse sequences can be used in design of two-dimensional solid state NMR experiments that use powdered dephased antiphase coherence (γ preparation) to encode chemical shifts in the indirect dimension. Both components of this chemical shift encoded gamma-prepared states can be refocused into inphase coherence by a recoupling element. This helps to achieve sensitivity enhancement in 2D NMR experiments by quadrature detection.

Keywords

MAS; Recoupling; Gamma preparation; Quadrature detection; Hartmann–Hahn matching

1. Introduction

Nuclear magnetic resonance (NMR) spectroscopy opens up the possibility of studying insoluble protein structures such as membrane proteins, fibrils, and extracellular matrix proteins which are difficult to analyze using conventional atomic-resolution structure determination methods, including liquid-state NMR and X-ray crystallography [2–6]. Recoupling pulse sequences that enable transfer of magnetization between coupled spins is the workhorse of all these experiments, either as a means to obtain structural information (e.g., internuclear distances) or as a means to improve resolution as building blocks in multiple-dimensional correlation experiments. The present paper describes some new methodology development for design of recoupling pulse sequences and demonstration of their use in so called gamma-preparation experiments [7,14] that enhance the sensitivity of 2D solid-state NMR experiments by a factor of $\sqrt{2}$.

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The paper is organized as follows. In Section 2, we describe a novel approach to homonuclear recoupling that recouple dipolar coupled spins under magic angle spinning (MAS) experiments. We call them three pulse recoupling. These experiments are broadband and robust to rf-inhomogeneity. This work extends recently developed techniques for broadband homonuclear recoupling as reported in the [14,1,16–18]. In Section 3, we describe these methods in the context of heteronuclear experiments. In the context of heteronuclear spins, the recoupling is achieved by matching the synchronized phase jumps on the two rf-channels (analogous to Hartmann–Hahn matching of the rf-power commonly seen in heteronuclear recoupling experiments [22]). In Section 4, we show how these recoupling blocks can be used to prepare a powder dephased, antiphase coherence and refocus both components of the chemical shift encoded γ prepared states (following t_1 evolution) into inphase coherence. Section 5, describes experimental verification of the proposed techniques.

2. Three pulse recoupling in homonuclear spins

Consider, two homonuclear spins I and S under magic angle spinning condition [20]. In a rotating frame, rotating with both the spins at their common Larmor frequency, the Hamiltonian of the spin system takes the form

$$H(t) = \omega_I(t)I_z + \omega_S(t)S_z + \omega_{IS}(t)(3I_zS_z - I \cdot S) + 2\pi A(t) \times (\cos\phi(t)F_x + \sin\phi(t)F_y), \quad (1)$$

where the operator $F_x = I_x + S_x$, and $\omega_I(t)$ and $\omega_S(t)$ represent the chemical shift for the spins I and S respectively and $\omega_{IS}(t)$ represents the time varying couplings between the spins under magicangle spinning. These interactions may be expressed as a Fourier series

$$\omega_\lambda(t) = \sum_{m=-2}^2 \omega_\lambda^m \exp(im\omega_r t), \quad (2)$$

where ω_r is the spinning frequency (in angular units), while the coefficients $\omega_\lambda(\lambda = I, S, IS)$ reflect the dependence on the physical parameters like the isotropic chemical shift, anisotropic chemical shift, the dipole–dipole coupling constant and through this the internuclear distance [23].

The term $I \cdot S$ in (1), commutes with the rf-field Hamiltonian, and in the absence of the chemical shifts, it averages to zero under MAS.

Consider the rf irradiation on homonuclear spin pair whose amplitude is chosen as $A(t) = \frac{C}{2\pi}$, where $C = n\omega_r$ and phase $\phi(t)$, such that

$$\dot{\phi}(t) = \frac{C\pi}{2n} \left(\delta\left(Ct - \frac{\pi}{2}\right) - \delta\left(Ct - \frac{3\pi}{2}\right) \right), \quad (3)$$

where $\delta(t)$ is a delta function ($\int_{-\varepsilon}^t f(\tau) \delta(\tau) d\tau = f(0)$ for all $\varepsilon > 0$, $t > 0$) and corresponds to instantaneous phase increment of 1 radian. See Fig. 1.

In the modulation frame, of the phase $\phi(t)$, the rf-field Hamiltonian takes the form

$$H^{rf}(t) = CF_x - \dot{\phi} F_z, \quad (4)$$

where C is in the angular frequency units and we choose $C \gg \omega_A(t), \omega_S(t), \omega_{IS}(t), \omega_r$. In the interaction frame of the irradiation along x axis, with the strength C , the chemical shifts of the spins are averaged out. The rf-field Hamiltonian of the spin system transforms to

$$H_I^{rf}(t) = - \underbrace{\frac{C\pi}{2n} \left(\delta\left(Ct - \frac{\pi}{2}\right) - \delta\left(Ct - \frac{3\pi}{2}\right) \right)}_{\dot{\phi}(t)} (F_z \cos(Ct) + F_y \sin(Ct)), \quad (5)$$

which accumulates an integral only when delta functions peak at $Ct = \frac{\pi}{2}$ and $Ct = \frac{3\pi}{2}$. The net rf rotation generated by $H_I^{rf}(t)$ is therefore $-\frac{\pi}{n} F_y$, which corresponds to a phase advance of $\frac{\pi}{2n}$ at $Ct = \frac{\pi}{2}$ and phase decrement of $\frac{\pi}{2n}$ at $Ct = \frac{3\pi}{2}$ (a negative phase decrement is multiplied by $\sin(\frac{3\pi}{2})$ which makes it a positive accumulation). See Fig. 1. A net rotation of $\frac{\pi}{n}$ in time $\tau_c = \frac{\tau_r}{n}$ corresponds to a net effective field of $\frac{\omega_r}{2}$. We have an effective field along $-y$ direction. The modulation frame of $\phi(t)$ returns to origin (see Figs. 2 and 3).

The above may be implemented with a three pulse sequence (for $n = 5$)

$$\left(\frac{\pi}{2}\right)_{0^\circ} (\pi)_{18^\circ} \left(\frac{\pi}{2}\right)_{0^\circ}.$$

where $\frac{\pi}{2}$ is the flip angle which takes $\frac{\tau_r}{4n}$ units of time with pulse amplitude of $C = n\omega_r$, so that in a rotor period τ_r , we have n of these units.

When pulse amplitude has inhomogeneity, then, in the modulation frame, of the phase $\phi(t)$, the rf-field Hamiltonian takes the form

$$H^{rf}(t) = C(1 + \varepsilon) F_x - \dot{\phi} F_z, \quad (6)$$

where C is in the angular frequency units and we choose $C \gg \omega_I(t), \omega_S(t), \omega_{IS}(t), \omega_r$. In the interaction frame of the irradiation along x axis, with the strength C , the rf-field Hamiltonian of the spin system transforms to

$$H_{I_a}^{rf}(t) = \varepsilon C F_x - \underbrace{\frac{C\pi}{2n} \left(\delta \left(Ct - \frac{\pi}{2} \right) - \delta \left(Ct - \frac{3\pi}{2} \right) \right)}_{\dot{\phi}(t)} (F_z \cos(Ct) + F_y \sin(Ct)), \quad (7)$$

which has an additional factor of $\varepsilon C F_x$, which accumulates to first order an evolution $\varepsilon 2\pi F_x - \frac{\pi}{n} F_y$, which for an inhomogeneity of $\varepsilon = .05$ and $n = 5$, corresponds to an evolution $\frac{\pi}{10} F_x - \frac{\pi}{5} F_y$ which limits the transfer efficiency. The inhomogeneity factor can be cancelled by following this pulse with a pulse of amplitude $-C$, where the phase is first decremented followed by increment, to accumulate same rf-Hamiltonian in the interaction frame of the x phase pulse.

$$\dot{\phi}(t) = \frac{C\pi}{2n} \left(-\delta \left(Ct - \frac{\pi}{2} \right) + \delta \left(Ct - \frac{3\pi}{2} \right) \right) \quad (8)$$

In the interaction frame of the irradiation along x axis, with the strength C , the rf-field Hamiltonian of the spin system transforms to

$$H_{I_b}^{rf}(t) = -\varepsilon C F_x + \underbrace{\frac{C\pi}{2n} \left(+\delta \left(Ct - \frac{\pi}{2} \right) - \delta \left(Ct - \frac{3\pi}{2} \right) \right)}_{\dot{\phi}(t)} (F_z \cos(Ct) - F_y \sin(Ct)), \quad (9)$$

Which accumulates an integral only when delta functions peak at $Ct = \frac{\pi}{2}$ and $Ct = \frac{3\pi}{2}$. The net rf rotation is therefore $-\frac{\pi}{n} F_y$ and $-C F_x$ cancel to first order.

The above may be implemented with a three pulse sequence (for $n = 5$)

$$\left(\frac{\pi}{2} \right)_{180^\circ} (\pi)_{180^\circ - 18^\circ} \left(\frac{\pi}{2} \right)_{180^\circ}.$$

The pulse sequence takes the form

$$\left(\frac{\pi}{2} \right)_{0^\circ} (\pi)_{18^\circ} \left(\frac{\pi}{2} \right)_{0^\circ} \left(\frac{\pi}{2} \right)_{180^\circ} (\pi)_{162^\circ} \left(\frac{\pi}{2} \right)_{180^\circ}.$$

We have calculated $\int_0^{\tau_c} H_{I_a}^{rf}(t)dt$ and $\int_0^{\tau_c} H_{I_b}^{rf}(t)dt$, which are first order contributions to generated rotation by time varying Hamiltonian $H_{I_a}^{rf}(t)$ and $H_{I_b}^{rf}(t)$. We can calculate the second order terms to write the total evolution as

$$\exp \left(\int_0^{\tau_c} H_{I_a}^{rf}(t)dt + \frac{1}{2} \int_0^{\tau_c} [H_{I_a}^{rf}(t), \int_0^t H_{I_a}^{rf}(\tau)d\tau]dt \right).$$

Let $u(t)$ be a unit step function that is zero for $t = 0$ and 1 for $t > 0$.

$$\int_0^t H_{I_a}^{rf}(\tau)d\tau = \varepsilon C F_x t - \frac{\pi}{2n} (u(t - \pi/2C) + u(t - 3\pi/2C)) F_y \quad (10)$$

$$\begin{aligned} \frac{1}{2} \int_0^{\tau_c} [H_{I_a}^{rf}(t), \int_0^t H_{I_a}^{rf}(\tau)d\tau] &= +i F_z \left(\frac{\pi \varepsilon C \tau_c}{2n} - \frac{\pi \varepsilon}{2n} \frac{\pi}{2} - \frac{\pi \varepsilon}{2n} \frac{3\pi}{2} \right) \\ &= 0 \end{aligned} \quad (11)$$

$$\int_0^t H_{I_b}^{rf}(\tau)d\tau = -\varepsilon C F_x t - \frac{\pi}{2n} (u(t - \pi/2C) + u(t - 3\pi/2C)) F_y \quad (12)$$

$$\begin{aligned} \int_0^{\tau_c} [H_{I_b}^{rf}(t), \int_0^t H_{I_b}^{rf}(\tau)d\tau] &= -i F_z \left(\frac{\pi \varepsilon C \tau_c}{2n} - \frac{\pi \varepsilon}{2n} \frac{\pi}{2} - \frac{\pi \varepsilon}{2n} \frac{3\pi}{2} \right) \\ &= 0 \end{aligned} \quad (13)$$

Therefore we prepare effective Hamiltonians $\varepsilon C F_x - \frac{\pi}{n\tau_c} F_y = \varepsilon C F_x - \frac{\pi}{\tau_c} F_y = \varepsilon C F_x - \frac{\omega_r}{2} F_y$, followed by the Hamiltonian $-\varepsilon C F_x - \frac{\omega_r}{2} F_y$. Toggling between them eliminates $\varepsilon C F_x$. The second order Hamiltonian is of order $\varepsilon \frac{\pi}{2} \omega_r F_z$. We have a recoupling field along $-\frac{\omega_r}{2} F_y + \varepsilon \frac{\pi}{2} \omega_r F_z$.

To evaluate the effect of recoupling field on the coupling Hamiltonian, we consider the pulse sequence

$$\left[\left(\frac{\pi}{2} \right)_{0^\circ} (\pi)_{180^\circ} \left(\frac{\pi}{2} \right)_{0^\circ} \left(\frac{\pi}{2} \right)_{180^\circ} (\pi)_{162^\circ} \left(\frac{\pi}{2} \right)_{180^\circ} \right]_n.$$

The rf-field alternates between $C(\cos \varphi(t) F_x + \sin \varphi(t) F_y)$ and $-C(\cos \varphi(t) F_x + \sin \varphi(t) F_y)$ every τ_c units of time, where φ is as in Fig. 1 and for $t \in [k\tau_c, (k+1)\tau_c]$, $\tau = t - k\tau_c$, $\tau \in [0, \tau_c]$. In the modulation frame of the rf-phase which alternates between $\varphi(t)$ and $-\varphi(t)$, rf-Hamiltonian alternates between $C F_x - \varphi(t) F_z$ and $-C F_x + \varphi(t) F_z$ every τ_c units of time where $\varphi(t)$ is as in Fig. 1. By transforming into the interaction frame of irradiation along x

axis which alternates between CF_x and $-CF_x$, we prepare $H_{I_a}^{rf}(\tau)$ and $H_{I_b}^{rf}(\tau)$ every τ_c units of time. The coupling Hamiltonian alternates between

$$H_{I+}^{DD}(t) = \frac{3}{2}\omega_{IS}(t)(I_z S_z + I_y S_y) + \frac{3}{2}\omega_{IS}(t)((I_z S_z - I_y S_y)\cos(2C\tau) + (I_z S_y + I_y S_z)\sin(2C\tau)),$$

(14)

$$H_{I-}^{DD}(t) = \frac{3}{2}\omega_{IS}(t)(I_z S_z + I_y S_y) + \frac{3}{2}\omega_{IS}(t)((I_z S_z - I_y S_y)\cos(2C(-\tau)) + (I_z S_y + I_y S_z)\sin(2C(-\tau))),$$

(15)

Now, transforming the coupling Hamiltonian in Eqs. (14) and (15), into the interaction frame of the rf-field Hamiltonian H_I^{rf} , we act with an effective field $-\frac{\omega_r}{2}F_y$, and only retain terms that give static contribution to the effective Hamiltonian, i.e., terms oscillating with frequency C are dropped and the residual Hamiltonian takes the form (neglecting the terms oscillating at frequency $2\omega_r$ as they are not recoupled)

$$H_{II}(t) = \kappa_h \{ \cos(\omega_r t) \cos(\omega_r t + \gamma) (I_n S_n - I_x S_x) + \sin(\omega_r t) \times \cos(\omega_r t + \gamma) (I_n S_x + I_x S_n) \}, \quad (16)$$

which averages to

$$\overline{H}_{II} = \frac{\kappa_h}{2} \{ \cos(\gamma) (I_n S_n - I_x S_x) + \sin(\gamma) (I_n S_x + I_x S_n) \}, \quad (17)$$

where $\kappa_h = \frac{3}{4\sqrt{2}} b_{IS} \sin(2\beta) \sin(2\beta)$, where b_{IS} is the dipole coupling constant and $n \hat{=}$ the effective direction

$$\hat{n} = \cos\theta \hat{z} + \sin\theta \hat{y},$$

where θ is of order $\pi\epsilon$ and $m \hat{=} \cos\theta \hat{y} - \sin\theta \hat{z}$, and $m \hat{\times} n \hat{=} x$. For small ϵ , $n \hat{=} \hat{z}$.

The rf-interaction frame, H_I^{rf} prepares an effective field $-\frac{\omega_r}{2}F_y$, every τ_c units of time. Transformation of the coupling Hamiltonian can be evaluated every τ_c units of time [14], by realizing that $\int_0^T U(t) J U(t) dt = \sum_k \int_{k-1\tau_c}^{k\tau_c} U_k(t) U((k-1)\tau_c) J U((k-1)\tau_c)' U_k(t)' dt$, where

$U((k-1)\tau_c)$ is the interaction frame propagator at time $(k-1)\tau_c$ and is same as evolution under effective field $-\frac{\omega_r}{2}F_y$ at this time, and $U_k(t)$ evolves in time $[(k-1)\tau_c, k\tau_c]$ with $U_k(t)=I+o(\frac{\omega_r}{2}\tau_c)$. For $\omega_r \ll C$, we can neglect the second factor and assume we evolve the coupling Hamiltonian under an effective field, $-\frac{\omega_r}{2}F_y$.

This pulse sequence is broadband as a large value of C averages out the chemical shift [16]. The high power pulse sequence is made robust to rf-inhomogeneity by combining phase increment and decrement units. The resulting pulse sequence is called **TPR, Three Pulse Recoupling**, as in Fig. 1.

In Fig. 1, we chose $C = 50$ KHz and $\omega_r = 10$ kHz which gives $n = 5$. We can use TPR with larger spinning frequencies. $C = 100$ kHz and $\omega_r = 20$ kHz which gives $n = 5$. Similarly $C = 120$ kHz and $\omega_r = 40$ kHz which gives $n = 3$. In the latter two cases, large power on the carbon can help in decoupling proton-carbon interactions so a separate decoupling field on proton may not be needed.

We can evaluate the effect of TPR pulse sequence on the chemical shift anisotropy in the interaction frame of irradiation along x axis which alternates between CF_x and $-CF_x$. The chemical shift anisotropy of spin I can be expressed as $(\omega_I^{\pm 1} \exp(\pm i\omega_r) + \omega_I^{\pm 2} \exp(\pm i2\omega_r))I_z$, we can decompose the operator $I_z = I^+ + I^-$, where $I^\pm = I_z \pm iI_y$, where $\exp(-iCI_x t)I^\pm \exp(+iCI_x t) = \exp(\pm iCt)(I^\pm)$. Using this, For $n = 5$, the CSA averages every two rotor periods, where TPR toggles between $\pm C$ every τ_c . Proceeding to interaction frame, H_I^{rf} , by acting with an effective field $-\frac{\omega_r}{2}F_y$, we find that for $n = 6$, the CSA averages to zero in first order.

The effective evolution resulting from the pulse sequence,

$$\left(\frac{\pi}{2}\right)_{0^\circ} (\pi)_\alpha \left(\frac{\pi}{2}\right)_{0^\circ},$$

can be directly evaluated using pauli matrices σ_α .

$$\cos\frac{\pi}{4}I - i2\sin\frac{\pi}{4}\sigma_x (-i2(\cos\alpha\sigma_x + \sin\alpha\sigma_y)) \cos\frac{\pi}{4}I - i2\sin\frac{\pi}{4}\sigma_x = -(\cos\alpha I + i2\sin\alpha\sigma_y) \left(\frac{\pi}{2}\right)_{180^\circ} (\pi)_{180-\alpha} \left(\frac{\pi}{2}\right)_{180^\circ},$$

is evaluated as

$$\cos\frac{\pi}{4}I + i2\sin\frac{\pi}{4}\sigma_x (i2(\cos\alpha\sigma_x - \sin\alpha\sigma_y)) \cos\frac{\pi}{4}I + i2\sin\frac{\pi}{4}\sigma_x = -(\cos\alpha I + i2\sin\alpha\sigma_y)$$

The resulting propagator on two spins is $\exp(i2aF_y)$, an effective rotation on two spins along $-y$ direction, with $2a$ flip angle, where a is radian equivalent of degrees as understood. For the presented sequence in above section $a = 18^\circ$, i.e. $\frac{\pi}{2n}$, for $n = 5$, as in Fig. 2.

Let, $\exp(-i \int_0^t H(\tau) d\tau)$ denote Unitary propogator generated by time varying Hamiltonian H . We can evaluate the evolution

$$V(t) = \exp \left(-i \int_0^t H_{I_a}^r d\tau \right) = \exp(iCF_x t) \exp(i\phi(t)F_z) U(t).$$

where $U(t)$ is evolution of the pulse sequence $(\frac{\pi}{2})_{0^\circ} (\pi)_\alpha (\frac{\pi}{2})_{0^\circ}$. For $0 \leq t \leq \frac{\tau_c}{4}$, we have, $\phi(t) = 0$ and $U(t) = \exp(-iCF_x t)$, resulting in $V(t) = I$. For $\frac{\tau_c}{4} < t \leq \frac{3\tau_c}{4}$, we have $\phi(t) = \alpha$, $\theta = Ct - \frac{C\tau_c}{4}$,

$$V(t) = \exp \left(iF_x \left(\frac{\pi}{2} + \theta \right) \right) \exp(i\alpha F_z) \exp(-i(F_x \cos \alpha + F_y \sin \alpha)\theta) \exp \left(-iF_x \frac{\pi}{2} \right) \quad (18)$$

$$= \exp \left(iF_x \frac{\pi}{2} \right) \exp(i\alpha F_z) \exp \left(-iF_x \frac{\pi}{2} \right) \quad (19)$$

$$= \exp \left(iF_x \frac{\pi}{2} \right) \exp(i\alpha F_z) \exp \left(-iF_x \frac{\pi}{2} \right) = \exp(i\alpha F_y) \quad (20)$$

For $\frac{3\tau_c}{4} < t \leq \tau_c$, we have $\phi(t) = 0$,

$$V(t) = \exp \left(iF_x \left(\frac{3\pi}{2} \right) \right) \exp(-i(F_x \cos \alpha + F_y \sin \alpha)\pi) \exp \left(-iF_x \frac{\pi}{2} \right) \\ = \exp(i2\alpha F_y) \quad (21)$$

We can calculate the same for the phase decrement sequence

$$W(t) = \exp \left(-i \int_0^t H_{I_a}^r dt \right) = \exp(-iCF_x t) \exp(i\phi(t)F_z) U(t).$$

where $U(t)$ is evolution of the pulse sequence $(\frac{\pi}{2})_{180^\circ} (\pi)_{180-\alpha} (\frac{\pi}{2})_{180^\circ}$. For $0 \leq t \leq \frac{\tau_c}{4}$, we have, $\phi(t) = 0$ and $U(t) = \exp(iCF_x t)$, resulting in $V(t) = I$. For $\frac{\tau_c}{4} < t \leq \frac{3\tau_c}{4}$, we have $\phi(t) = -\alpha$, $\theta = t - \frac{\tau_c}{4}$,

$$W(t) = \exp\left(-iF_x\left(\frac{\pi}{2} + \theta\right)\right) \exp(-i\alpha F_z) \exp(i(F_x \cos\alpha - F_y \sin\alpha)\theta) \exp\left(iF_x\frac{\pi}{2}\right) \quad (22)$$

$$= \exp\left(-iF_x\frac{\pi}{2}\right) \exp(-i\alpha F_z) \exp\left(iF_x\frac{\pi}{2}\right) = \exp(i\alpha F_y) \quad (23)$$

For $\frac{3\tau_c}{4} < t \leq \tau_c$, we have $\varphi(t) = 0$,

$$W(t) = \exp\left(-iF_x\left(\frac{3\pi}{2}\right)\right) \exp(i(F_x \cos\alpha - F_y \sin\alpha)\theta) \exp\left(iF_x\frac{\pi}{2}\right) \\ = \exp(i2\alpha F_y) \quad (24)$$

3. Phase matching and heteronuclear recoupling

Consider two coupled heteronuclear spins I and S under magic angle spinning condition [22]. The spins are irradiated with rf fields at their Larmor frequencies along say the x direction. In a double-rotating Zeeman frame, rotating with both the spins at their Larmor frequency, the Hamiltonian of the system takes the form

$$H(t) = \omega_I(t)I_z + \omega_S(t)S_z + \omega_{IS}(t)2I_zS_z + H^rf(t), \quad (25)$$

where $\omega_I(t)$, $\omega_S(t)$, and $\omega_{IS}(t)$ represent time-varying chemical shifts for the two spins I and S and the coupling between them, respectively. These interactions can be expressed as a

Fourier series $\omega_\lambda(t) = \sum_{m=-2}^2 \omega_\lambda^m \exp(im\omega_r t) \exp(im\varphi(t))$, where ω_r is the spinning frequency (in angular units), while the coefficients ω_λ , ($\lambda = I, S$) reflect the dependence on the physical parameters like the isotropic chemical shift, anisotropic chemical shift, the dipole-dipole coupling constant and through this the internuclear distance [23,24].

Consider the rf irradiation on heteronuclear spin pair, where amplitude on spin I and S is chosen as $A_\lambda(t) = \frac{C}{2\pi}$ ($\lambda = I, S$) such that $C = n\omega_r$, and phase modulation, given by

$$\dot{\phi}_I(t) = \frac{3C\pi}{4n} \left(\delta\left(Ct - \frac{\pi}{2}\right) - \delta\left(Ct - \frac{3\pi}{2}\right) \right) \quad (26)$$

$$\dot{\phi}_S(t) = \frac{C\pi}{4n} \left(\delta\left(Ct - \frac{\pi}{2}\right) - \delta\left(Ct - \frac{3\pi}{2}\right) \right) \quad (27)$$

where phase jump is three halves and half of the modulation considered in previous section. As a result, the effective fields prepared on two channels will be $\frac{3\omega_r}{4}$ and $\frac{\omega_r}{4}$, with average $\frac{\omega_r}{2}$, which will recouple a double quantum Hamiltonian. In implementation, this would correspond to a phase increment which is three halves and half of the phase increment in previous section, i.e., 27° and 9° . To mitigate the effect of inhomogeneity of rf-field, the basic pulse unit is accompanied with a phase decrement unit. In nutshell the pulse sequence on channels I and S (say C^{13} and N^{15}) is following respectively.

$$\left(\frac{\pi}{2}\right)_{0^\circ} (\pi)_{27^\circ} \left(\frac{\pi}{2}\right)_{0^\circ} \left(\frac{\pi}{2}\right)_{180^\circ} (\pi)_{153^\circ} \left(\frac{\pi}{2}\right)_{180^\circ}. \quad (28)$$

$$\left(\frac{\pi}{2}\right)_{0^\circ} (\pi)_{9^\circ} \left(\frac{\pi}{2}\right)_{0^\circ} \left(\frac{\pi}{2}\right)_{180^\circ} (\pi)_{171^\circ} \left(\frac{\pi}{2}\right)_{180^\circ}. \quad (29)$$

In the frame of the rf-field along x axis, that toggles between $\pm C(I_x + S_x)$, the coupling Hamiltonian is averaged to

$$H_{I\pm}^{DD}(t) = \omega_{IS}(t)(I_z S_z + I_y S_y) + \omega_{IS}(t)((I_z S_z - I_y S_y)\cos(2C\tau) \pm (I_z S_y + I_y S_z)\sin(2C\tau)), \quad (30)$$

With effective rf-field $-\frac{3\omega_r}{4}I_y - \frac{\omega_r}{4}S_y$ written as $-\omega_r \frac{(I_y + S_y)}{2} - \frac{\omega_r}{2} \frac{(I_y - S_y)}{2}$, the coupling Hamiltonian is further averaged to

$$\overline{H}_{II} = \kappa_d \{ \underbrace{(I_z S_z - I_x S_x)\cos(\gamma) + (I_x S_z + I_z S_x)\sin(\gamma)} \}. \quad (31)$$

We call the above experiments heteronuclear **TPR**.

4. Gamma-preparation

We now show how **TPR** recoupling pulse sequences can be used in design of two-dimensional solid state NMR experiments that use powdered dephased antiphase coherence (γ preparation) to encode chemical shifts in the indirect dimension. Both components of this chemical shift encoded gamma-prepared states can be refocused into inphase coherence by a recoupling element. This helps to achieve sensitivity enhancement in 2D NMR experiments by quadrature detection.

Notation

Let $S_a(\beta, \gamma)$ denote the rotation of operator S_a around the axis β by angle γ , where $a, \beta \in \{x, y, z\}$, i.e., $S_a(\beta, \gamma) = \exp(-i\gamma S_\beta) S_a \exp(i\gamma S_\beta)$. For example $S_x(z, \gamma) = S_x \cos \gamma + S_y \sin \gamma$. It is straightforward to verify relations of the following kind

$$[-iS_x(\beta, \gamma), -iS_y(\beta, \gamma)] = -iS_z(\beta, \gamma).$$

It also follows from definition that for any unitary transformation U ,

$$US_\alpha(\beta, \gamma)U' = S_{U\alpha U'}(U\beta U', \gamma),$$

where $S_{U\alpha U'}(U\beta U', \gamma)$, denotes rotation of operator $US_\alpha U'$ around $US_\beta U'$.

Let the unit vectors l, m, n constitute a right handed coordinate system ($l \times m = n$). Then

$$\mathcal{H}_{zQ}^l(\gamma) = I_m S_m(l, \gamma) + I_n S_n(l, \gamma) = I_m(l, -\gamma) S_m + I_n(l, -\gamma) S_n. \quad (32)$$

and

$$\mathcal{H}_{DQ}^l(\gamma) = I_m S_m(l, \gamma) - I_n S_n(l, \gamma) = I_m(l, \gamma) S_m - I_n(l, \gamma) S_n. \quad (33)$$

are used to denote the zero quantum and multiple (double) quantum operators.

Consider the recoupling effective field $-\frac{\omega_r}{2}F_y$ as in Section 2, obtained using **TPR** pulse sequence. This prepares a recoupling Hamiltonian,

$$\mathcal{H}_{DQ}^y(\gamma) = I_z S_z(y, \gamma) - I_x S_x(y, \gamma). \quad (34)$$

and with bracketing $\frac{\pi}{2}$ pulses along $-x$ and x , we prepare an Hamiltonian ($z \bar{z} = -z$),

$$\mathcal{H}_{DQ}^{\bar{z}}(\gamma) = I_y S_y(\bar{z}, \gamma) - I_x S_x(\bar{z}, \gamma). \quad (35)$$

Now, consider the following experiment,

$$I_x \xrightarrow{I} \xrightarrow{(\mathcal{H}_{DQ}^{\bar{z}}(\gamma))} \xrightarrow{\pi} -2I_z S_y(\bar{z}, \gamma) \xrightarrow{II} \xrightarrow{\omega_s S_z} -2I_z S_y(\bar{z}, \gamma - \omega_s t_1) \xrightarrow{III} \xrightarrow{(H_{DQ}^{\bar{z}}(\gamma'))} \xrightarrow{\pi} -I_x(z, \gamma - \gamma' - \omega_s t_1) \quad (36)$$

If the preparation Hamiltonian $\mathcal{H}_{DQ}^{\bar{z}}(\gamma)$ is applied for an integral number of rotor periods, then

$$\gamma' = \gamma + \omega_r t_1.$$

The final state following the refocusing is

$$-I_x(z, -(\omega_r + \omega_s)t_1) = -(I_x \cos(-(\omega_r + \omega_s)t_1) + I_y \sin(-(\omega_r + \omega_s)t_1)).$$

Remark 1

The magnetization in t_1 evolution precesses with chemical shift, $-(\omega_r + \omega_s)$, where ω_s is measured with respect to carrier frequency. The Gamma-Preparation peaks in the 2D spectra are reflected around the carrier frequency and further downshifted by rotor frequency. The spectra is obtained as described in the following and shown in Fig. 4B for the $^{13}\text{C}_\alpha$ - $^{13}\text{C}_\beta$ correlation experiment.

Fig. 4B shows how two Gamma-Preparation experiments are processed. The Gamma-Preparation magnetization after the t_1 evolution is given by $-I_x \cos(-(\omega_r + \omega_s)t_1) - I_y \sin(-(\omega_r + \omega_s)t_1)$. Following this with a π pulse in a second experiment gives $-I_x \cos(-(\omega_r + \omega_s)t_1) + I_y \sin(-(\omega_r + \omega_s)t_1)$. In Fig. 4B, π pulse is implemented with two consecutive $\frac{\pi}{2}$ pulses whose phase cancels to give an echo signal, and adds to give an anti-echo signal. Adding the two results and subtracting them, gives magnetization $-2I_x \cos(-(\omega_r + \omega_s)t_1)$ and $-2I_y \sin(-(\omega_r + \omega_s)t_1)$, prior to the t_2 evolution. Following t_2 evolution, recorded signal has the form, $s_A(t_1, t_2) = 2 \cos(-(\omega_s + \omega_r)t_1) \exp(-j\omega t_2)$ and $s_B(t_1, t_2) = 2 \sin(-(\omega_s + \omega_r)t_1) \exp(-j\omega t_2)$, for the two experiments respectively. TPPI processing of both, gives two absorptive 2D-spectra. Fig. 7A shows one of these spectra. The two spectra can be phased and added to get sensitivity enhancement as shown in Fig. 7B and C.

We can apply Gamma preparation to $^{13}\text{C}(\text{I})$ - $^{15}\text{N}(\text{S})$ Heteronuclear correlation experiment, where we prepare antiphase coherence of the S spin N^{15} that evolves during t_1 . The preparation can be done with an effective field $-\omega_r S_y$, which excited both double and zero quantum coherence frames and creates an effective Hamiltonian $2I_{zS} S_x(y, \gamma)$ which can be tilted to $2I_{zS} S_y(z, -\gamma)$, with bracketing $\frac{\pi}{2}$ pulses. The effective field can be obtained with a TPR pulse sequence.

$$\left(\frac{\pi}{2}\right)_{0^\circ} (\pi)_{36^\circ} \left(\frac{\pi}{2}\right)_{0^\circ} \left(\frac{\pi}{2}\right)_{180^\circ} (\pi)_{144^\circ} \left(\frac{\pi}{2}\right)_{180^\circ}. \quad (37)$$

$$\left(\frac{\pi}{2}\right)_{0^\circ} (\pi)_{0^\circ} \left(\frac{\pi}{2}\right)_{0^\circ} \left(\frac{\pi}{2}\right)_{180^\circ} (\pi)_{0^\circ} \left(\frac{\pi}{2}\right)_{180^\circ}. \quad (38)$$

on the ^{15}N and ^{13}C channels respectively. We call this TPR1 in Fig. 4C. After t_1 evolution, the refocusing is done with the pulse sequence described in the main text which is

$$\left(\frac{\pi}{2}\right)_{0^\circ} (\pi)_{27^\circ} \left(\frac{\pi}{2}\right)_{0^\circ} \left(\frac{\pi}{2}\right)_{180^\circ} (\pi)_{153^\circ} \left(\frac{\pi}{2}\right)_{180^\circ}. \quad (39)$$

$$\left(\frac{\pi}{2}\right)_{0^\circ} (\pi)_{9^\circ} \left(\frac{\pi}{2}\right)_{0^\circ} \left(\frac{\pi}{2}\right)_{180^\circ} (\pi)_{171^\circ} \left(\frac{\pi}{2}\right)_{180^\circ}. \quad (40)$$

on ^{13}C and ^{15}N channels respectively. We call this TPR2 in Fig. 4C. Now, consider the following experiment, starting from magnetization on I spin ^{13}C ,

$$I_x \xrightarrow{I} (I_y S_y(\bar{z}, \gamma))_\pi \rightarrow -2I_z S_y(\bar{z}, \gamma) \xrightarrow{II} -2I_z S_y(\bar{z}, \gamma - \omega_s t_1) \xrightarrow{III} -I_x(z, \gamma - \gamma' - \omega_s t_1). \quad (41)$$

The processing steps are same as described above for homonuclear experiment. The pulse sequence is as shown in Fig. 4C.

5. Experimental results

All experiments [14] were performed on a 400 MHz spectrometer (^1H Larmor frequency of 400 MHz) equipped with a triple resonance 4 mm probe. Uniformly ^{13}C , ^{15}N -labeled sample of alanine and uniformly ^{13}C , ^{15}N -labeled sample of glycine was used in the full volume of standard 4 mm rotor at ambient temperature using $\frac{\omega_r}{2\pi} = 10$ kHz sample spinning, for homonuclear and heteronuclear experiments respectively. The experiments used 3s recycling delay. All 2D experiments were processed using TPPI processing.

Top panel of Fig. 5A shows the build up curve for transfer of magnetization, starting from one of the carbons, for $^{13}\text{C}_\alpha - ^{13}\text{C}_\beta$ correlation experiment with **TPR** as the recoupling element. The experiment uses an initial ramped CP for ^1H to ^{13}C cross polarization. The **TPR** recoupling block is designed for a nominal power of 50 kHz as described in the text. In experiment, this power is optimized to give maximum transfer efficiency. The experiment used CW decoupling on protons of $\frac{\omega_{rf}^H}{2\pi} = 100$ kHz during the transfer. Bottom panel of Fig. 5A shows a $^{13}\text{C}_\alpha - ^{13}\text{C}_\beta$ 2D correlation spectrum obtained using the **TPR** as the recoupling element. The experiment used 1024 points in both direct and indirect dimension with dwell time of 25 μs .

Top panel of Fig. 6 shows the build up of transfer of magnetization, shown every 8 rotor periods for the $^{13}\text{C}_\alpha \rightarrow ^{15}\text{N}$ experiment with **TPR** as the recoupling element. The experiment uses an initial ramped CP for ^1H to ^{13}C cross polarization. The **TPR** recoupling block is designed for a nominal power of 50 kHz as described in the text. In experiment, this power is optimized to give maximum transfer efficiency. The experiment used CW decoupling on protons of $\frac{\omega_{rf}^H}{2\pi} = 100$ kHz during the transfer. Middle panel of Fig. 6 shows the

build up of transfer of magnetization, shown every 8 rotor periods for the $^{15}\text{N} \rightarrow ^{13}\text{C}$ experiment with **TPR** as the recoupling element. The experiment uses an initial ramped CP for ^1H to ^{15}N cross polarization. The **TPR** block used for this transfer is same as above. Bottom panel of Fig. 6 shows the 2D spectrum for $^{13}\text{C}_\alpha$ - ^{15}N experiment with **TPR** as the recoupling element. The magnetization precesses on ^{15}N during indirect evolution. The experiment used 1024 points in both direct and indirect dimension with dwell time of 25 μs .

Top panel of Fig. 7 shows the 2D gamma-preparation spectrum for the pulse sequence shown in Fig. for $^{13}\text{C}_\alpha$ - $^{13}\text{C}_\beta$ correlation as described in the text. The frequencies in the indirect dimension are reflected around the carrier and rotor down-shifted as described in the text. The carrier is at around 40 ppm. The experiment uses an initial ramped CP for ^1H to ^{13}C cross polarization, followed by gamma-preparation experiment with **TPR** as recoupling block, designed with a nominal power of 50 kHz as described in the text. The

experiment used CW decoupling on protons of $\frac{\omega_H}{2\pi} = 100 \text{ kHz}$ during the transfer. Middle panel of Fig. 7 shows the comparison of peak intensity of a slice through a cross-peak of a straight $^{13}\text{C}_\alpha$ - $^{13}\text{C}_\beta$ correlation obtained with **TPR**, with magnetization evolving on C_β during indirect evolution as in bottom panel of Fig. 5, vs a slice through a gamma-preparation cross peak, where magnetization begins from C_β and precesses on C_α during t_1 . The gamma-preparation peak was processed as shown in 4B. Bottom panel of Fig. 7 shows the comparison of peak intensity of a slice through a cross-peak of a straight $^{13}\text{C}_\alpha$ - $^{13}\text{C}_\beta$ correlation obtained with **TPR**, as in bottom panel of Fig. 5, with magnetization evolving on C_α during indirect evolution, vs a slice through a gamma-preparation cross peak, where magnetization begins from C_α and precesses on C_β during t_1 . The gamma-preparation peak was processed as shown in Fig. 4B. In both cases, we see noticeable enhancement in sensitivity. Gamma-preparation experiment requires collecting two scans as shown in Fig. 4. For sensitivity comparison, we doubled the number of scans in a straight $^{13}\text{C}_\alpha$ - $^{13}\text{C}_\beta$ correlation obtained with **TPR**, as in top panel of Fig. 5. The experiment used 1024 points in both direct and indirect dimension with dwell time of 25 μs .

Fig. 8 shows the gamma preparation peak for the 2D heteronuclear experiment which prepares an antiphase coherence on nitrogen to encode its chemical shift with preparation and refocusing done with TPR pulse sequences with power of 50 kHz, with rotor frequency of 10 kHz and $n = 5$. The carrier on nitrogen is on-resonance. The pulse sequence is as shown in Fig. 4C with preparation and refocusing pulse sequences labelled as TPR 1 and TPR 2. The experiment used 1024 points in both direct and indirect dimension with dwell time of 25 μs . Choice of a different preparation pulse is made to reduce preparation time by half.

6. Conclusion

In this paper we introduced a class of recoupling pulse sequences, which rest on the principle of second oscillating field. A strong field is used to eliminate chemical shifts and make the sequence broadband. Furthermore this strong rf-field is used to demodulate a second oscillating field which performs recoupling. In our design, the second oscillating field comes about by principled phase changes which are described in the paper. The

recoupling sequences presented in the paper for homonuclear and heteronuclear spin systems are broadband and robust to rf-inhomogeneity. Furthermore, they are easy to program and implement on the spectrometer. The sequence have been used as building block for Gamma-preparation experiments that perform simultaneous transfer of both the components of magnetization in a transfer experiment and hence enhance sensitivity by Quadrature detection.

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Further reading

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Fig. 1.

Top left panel shows ramp of phase in Eq. (5). The Top right panel shows time derivative of phase in Eq. (5). Area under this curve gives the total phase change. The bottom panel shows the accumulation of phase area at the crossed points when the magnetization is rotated in the interaction frame of CF_x as in Eq. (5).

Fig. 2.

Top panel in the figure shows the build up of transfer of magnetization in a basic ^{13}C – ^{13}C correlation experiment on a 400 MHz (proton frequency) static field, using the **TPR** pulse unit with 18° as phase increment and no compensating phase decrement. Simulation uses internuclear distance of 1.52 Å and powder averaging. *a*, *b*, *c* corresponds to inhomogeneity value ε of 0, .01 and .05 respectively. Middle Panel in the figure shows the build up basic ^{13}C – ^{13}C correlation experiment using the **TPR** pulse unit with 18° as phase increment combined with an 18° decrement unit. *a*, *b*, *c*, *d* corresponds to inhomogeneity value ε of 0, .01, .05, and .1 respectively. In practice, the rf-inhomogeneity results in a weighted sum of these different ε . Offset of spin pair is assumed to be on resonance. Bottom panel in the figure shows the build up of basic ^{13}C – ^{13}C correlation experiment using the **TPR** pulse unit with 18° as phase increment combined with an 18° decrement unit, with different chemical shift of the target spin. *a*, *b*, *c*, *d*, corresponds to chemical shift of 0, 5, 10 and 15 kHz on the target spin. In the bottom panel, we include a CSA value of 8.9 and 13.9 ppm for the two spins respectively with anisotropy parameter .13 and .98, representing the C_α – C_β spin pair in alanine respectively.

Fig. 3.

Top panel in the figure shows the build up basic ^{13}C - ^{15}N correlation experiment on a 400 mHz (proton frequency) static field, using the **TPR** pulse unit with 27° and 9° as phase increment and no compensating phase decrement on ^{13}C and ^{15}N respectively. *a*, *b*, *c* corresponds to inhomogeneity value ε of 0, .01 and .05 on Carbon channel. Middle Panel in the figure shows the build up using the **TPR** pulse unit with compensating phase decrement unit. Bottom panel in the figure shows the build up of basic ^{13}C - ^{15}N correlation experiment using the **TPR** pulse unit, with different chemical shift of the ^{13}C spin. *a*, *b*, *c*, *d*, corresponds to chemical shift of 0, 5, 7.5 and 10 kHz of the ^{13}C spin.

Fig. 4.

(A) shows the pulse sequence for a $^{13}\text{C}_\alpha$ - $^{13}\text{C}_\beta$ correlation experiment with **TPR** as the recoupling element. (B) Shows the pulse sequence for a $^{13}\text{C}_\alpha$ - $^{13}\text{C}_\beta$ correlation experiment using gamma preparation, with **TPR** as the recoupling element. (C) Shows the pulse sequence for a $^{13}\text{C}_\alpha$ - ^{15}N correlation experiment using gamma preparation, with **TPR** as the recoupling element. In (C) the last $\frac{\pi}{2}$ pulse on the carbon is toggled from $-x$ to x during acquisition of second scan which is added and subtracted with first scan as described in (B).

Fig. 5.

Top panel shows the build up curve for transfer of magnetization, shown every 2 rotor periods, at 10 kHz spinning, starting from one of the carbons, for $^{13}\text{C}_\alpha\text{-}^{13}\text{C}_\beta$ correlation experiment, in uniformly labelled sample of Alanine, with **TPR** as the recoupling element as described in the text. Bottom panel shows a $^{13}\text{C}_\alpha\text{-}^{13}\text{C}_\beta$ 2D correlation spectrum obtained using the **TPR** as the recoupling element.

Fig. 6.

Top panel shows the build up of transfer of magnetization, shown every 8 rotor periods, at 10 kHz spinning, for the $^{13}\text{C}_\alpha \rightarrow ^{15}\text{N}$ experiment, in uniformly labelled sample of glycine, with **TPR** as the recoupling element as described in text. Middle panel shows the build up of transfer of magnetization, shown every 8 rotor periods for the $^{15}\text{N} \rightarrow ^{13}\text{C}$ experiment with same **TPR** as the recoupling element. Bottom panel shows the 2D spectrum for $^{13}\text{C}_\alpha$ - ^{15}N experiment with **TPR** as the recoupling element. The magnetization precesses on ^{15}N during indirect evolution.

Fig. 7.

Top panel shows the 2D gamma-preparation spectrum for the pulse sequence shown in figure for $^{13}\text{C}_\alpha\text{--}^{13}\text{C}_\beta$ correlation as described in the text. The frequencies in the indirect dimension are reflected around the carrier and down-shifted by rotor frequency of 10 kHz (100 ppm at 400 kHz) as described in the text. The carrier is at around 40 ppm. Middle panel shows the comparison of peak intensity of a slice through a cross-peak of a straight $^{13}\text{C}_\alpha\text{--}^{13}\text{C}_\beta$ correlation obtained with **TPR**, with magnetization evolving on C_β during indirect evolution as in bottom panel of Fig. 5, vs a slice through a larger gamma-preparation cross peak, where magnetization begins from C_β and precesses on C_α during t_1 . Bottom panel shows the comparison of peak intensity of a slice through a cross-peak of a straight $^{13}\text{C}_\alpha\text{--}^{13}\text{C}_\beta$ correlation obtained with **TPR**, as in bottom panel of Fig. 5, with magnetization evolving on C_α during indirect evolution, vs a slice through a larger gamma-preparation cross peak, where magnetization begins from C_α and precesses on C_β during t_1 .

Fig. 8.

Figure shows the gamma preparation peak for the 2D heteronuclear experiment which prepares an antiphase coherence on nitrogen to encode its chemical shift with preparation and refocussing done with TPR pulse sequence.