Fourier synthesis techniques for NMR spectroscopy in inhomogeneous fields

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This paper describes a method for synthesizing spin rotations with arbitrary space dependence on a sample of noninteracting spin $\frac{1}{2}$ by using nonselective radio frequency pulses and pulsed field gradients. This method is used to map out spatial distribution of inhomogeneous B_0 field and to engineer a space dependent evolution of spins that cancels the space dependent phase spins acquire when precessing in an inhomogeneous magnetic field. The technique allows one to record high resolution spectra in inhomogeneous magnetic field by using only time varying linear gradients and rf fields and is expected to find applications in *ex situ* NMR. © *2008 American Institute of Physics*.
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I. INTRODUCTION

High resolution NMR experiments require extremely homogeneous magnetic fields to obtain chemical shift and J coupling information of nuclei, as these interactions are orders of magnitude smaller than the main Zeeman coupling to the external field B_0. Achieving such homogeneity is not trivial, especially over relatively large sample volumes and when dealing with spatially heterogeneous tissues or employing remote NMR arrangements. Number of methods have recently been proposed to compensate for the B_0 inhomogeneity using radio frequency (rf) fields.[1–8] These either use an inhomogeneous rf field, matched to the inhomogeneity of the B_0 field[5] or use field gradients along with rf pulses to compensate for the phase that will be accumulated due to inhomogeneous B_0 magnetic field in one dimension.[8] In our recent work,[1] we showed that phase compensation in the presence of arbitrary three dimensional (3D) field inhomogeneities is possible using spatially nonselective rf pulse sequences and linear time varying 3D gradients. We presented a constructive method, "the Fourier synthesis design technique" for synthesizing the desired space dependent rotations. In all previous methods, the spatial profile of B_0 field inhomogeneities need to be mapped out *a priori*. In this paper, we show how to design a sequence of experiments which use rf pulse sequences and time varying gradients as probes to progressively learn about the spatial distribution of field inhomogeneities in three dimensions. These experiments progressively work on narrowing the linewidth of the resonance. The experiments are designed so that reducing the linewidths below a certain threshold is the same as estimating the field profile to a desired level of confidence. The parameters of the rf pulse sequence and the time varying gradients that minimize the linewidth of the resonance also parametrize the inhomogeneous field distribution and can be used to correct for it. The same pulse sequence can then be used as a building block for acquiring high resolution NMR spectra in inhomogeneous fields. These proposed methods can potentially replace dedicated shim coils in inexpensive magnets for specialized applications of traditional NMR or imaging experiments in materials science, chemical engineering, process, product, and quality control.

II. THEORY

In a static magnetic field B_0 in the z direction, the spin magnetization $M(\mathbf{r})$ at the spatial location $\mathbf{r}=(x,y,z)$ evolves according to the Bloch equation

$$\frac{dM(\mathbf{r})}{dt} = \gamma\{(1-\sigma)(B_0+\delta B(\mathbf{r})+\mathbf{G}(t)\cdot\mathbf{r})Z + B_x(t)X + B_y(t)Y\}M(\mathbf{r}), \quad (1)$$

where $\mathbf{G}(t)=(G_x(t),G_y(t),G_z(t))$ represents the 3D time varying gradient vector, (X,Y,Z) represents generators of rotations around the x, y, and z axes, and $B_x(t)=B_{\mathrm{rf}}(t)\cos(\omega_0 t+\psi(t))$ and $B_y(t)=B_{\mathrm{rf}}(t)\sin(\omega_0 t+\psi(t))$ represent the x and y components of the rf field, respectively. γ and σ represent the gyromagnetic ratio and the chemical shift of the nuclei. Here, $\omega_0=\gamma B_0$ is the nominal Larmor frequency and $B_{\mathrm{rf}}(t)$ and $\psi(t)$ are the amplitude and phase of the rf field. $\delta B(\mathbf{r})$ is the inhomogeneity of the B_0 field at spatial location $\mathbf{r}=(x,y,z)$, where $0<x<L_1$, $0<y<L_2$, and $0<z<L_3$, where L_1, L_2, and L_3 are the dimensions of the sample volume. We also assume that the strength of the maximum rf field is such that $B_{\mathrm{rf}} \gg \delta B(\mathbf{r})$. The assumption is made to ensure that rotations produced by rf pulses are uniform on the whole sample. This assumption is not necessary for the subsequent developments and can be relaxed by the use of broadband excitation rf pulses. In the absence of rf fields and gradients, the spins precessing at the location $\mathbf{r}$ will accumulate in time T, a phase evolution

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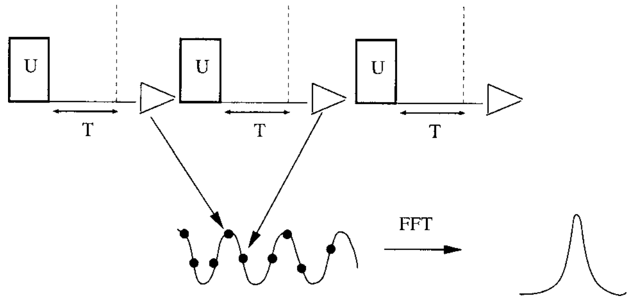

FIG. 1. The schematic of repeated application of the space dependent rotation $U(\mathbf{r})$ before the free precession of the spins for T units of time, followed by sampling of free induction decay (FID). The samples obtained after every T units of net evolution (represented as a solid dot) are then used to generate the Fourier transform of the signal.

$$\phi(\mathbf{r}) = \gamma(B_0 + \delta B(\mathbf{r}))(1-\sigma)T.$$

We assume that $\delta B(\mathbf{r}) \ll B_0$, and that the chemical shift σ is only ppm. For all practical purposes, we can neglect the term $(\sigma\gamma\delta B(\mathbf{r})T)$ and write

$$\phi(\mathbf{r}) = \gamma B_0(1-\sigma)T + \underbrace{\gamma\delta B(\mathbf{r})T}_{\delta\phi(\mathbf{r})}. \tag{2}$$

In our previous work,[1] we showed how to design a sequence of rf pulses and time varying gradients to synthesize arbitrary space dependent rotations, in particular, a rotation of the form

$$U(r) = \exp(-\delta\phi(r)Z).$$

The goal is to perform an experiment, as depicted in Fig. 1, where the unitary transformation $U(r)$ (which we simply denote as U in the Fig. 1 and refer to as the U block) is synthesized with gradients and pulses, followed by evolution of spins in an inhomogeneous field for a time T. The inhomogeneous phase accumulated by spin precession in an inhomogeneous field is exactly canceled by the rotation $U(r)$. The precession is sampled at this point and then the whole procedure is repeated. The resulting evolution of spins is only due to chemical shifts and construction of a spectrum, as depicted in Eq. (1), provides chemical shift information. The time T is chosen as the usual Nyquist dwell time dictated by the spectral width (SW). The $U(r)$ block is designed to avoid chemical shift evolution during its application. Synthesis of an appropriate $U(r)$ requires knowledge of $\delta B(r)$. We first recapitulate the main result of Pryor and Khaneja[1] of synthesizing $U(r)$, when $\delta B(r)$ or $\delta\phi(r)$ is known. We then show that the same procedure can be used to determine $\delta B(r)$ (which is the main contribution of this paper).

The phase $\delta\phi(\mathbf{r})$ is expressed as a constant, a component varying linearly with space and a nonlinear space component, i.e., we can express,

$$\delta\phi(\mathbf{r}) = c_0 + \mathbf{c}\cdot\mathbf{r} + \theta(\mathbf{r}),$$

where $\mathbf{c}=(c_1,c_2,c_3)$. The coefficients (c_0,c_1,c_2,c_3) can be determined by a least squares approximation of $\delta\phi(\mathbf{r})$ by the function $c_0+\mathbf{c}\cdot\mathbf{r}$, i.e., minimizing

$$f(c_0,c_1,c_2,c_3) = \int_0^{L_3}\int_0^{L_2}\int_0^{L_1} \|\delta\phi(\mathbf{r}) - (c_0 + \mathbf{c}\cdot\mathbf{r})\|^2 d^3r.$$

We get the optimal values of c_i, for $i=0,1,2,3$, by simply substituting $\partial f/\partial c_i=0$, which gives

$$\begin{bmatrix} \langle 1,x\rangle & \langle 1,y\rangle & \langle 1,z\rangle & \langle 1,1\rangle \\ \langle x,x\rangle & \langle x,y\rangle & \langle x,z\rangle & \langle x,1\rangle \\ \langle y,x\rangle & \langle y,y\rangle & \langle y,z\rangle & \langle y,1\rangle \\ \langle z,x\rangle & \langle z,y\rangle & \langle z,z\rangle & \langle z,1\rangle \end{bmatrix} \begin{bmatrix} c_1 \\ c_2 \\ c_3 \\ c_0 \end{bmatrix} = \begin{bmatrix} \langle 1,\delta\phi(\mathbf{r})\rangle \\ \langle x,\delta\phi(\mathbf{r})\rangle \\ \langle y,\delta\phi(\mathbf{r})\rangle \\ \langle z,\delta\phi(\mathbf{r})\rangle \end{bmatrix}, \tag{3}$$

where

$$\langle f,g\rangle = \int_0^{L_3}\int_0^{L_2}\int_0^{L_1} f(x,y,z)g(x,y,z)dxdydz$$

is the standard scalar product between functions. Then, $\theta(\mathbf{r}) = \delta\phi(\mathbf{r}) - \mathbf{c}\cdot\mathbf{r} - c_0$.

We can now expand $\theta(\mathbf{r})$ into a Fourier series. We use $\mathbf{k}$ to denote the triplet (k_x,k_y,k_z). We extend the domain of θ to create periodic boundary conditions. We define $\theta(x,y,z) = \theta(-x,y,z)$ for $-L_1<x<L_1$. Similarly for y and z. Note that $\theta(x,y,z)$ is now defined on $-L_1<x<L_1$ and $-L_2<y<L_2$ and $-L_3<z<L_3$ and can be expanded as

$$\theta(\mathbf{r}) = \sum_{\mathbf{k}\neq 0} a_{\mathbf{k}} \exp\left(i\frac{\pi k_x x}{L_1}\right)\exp\left(i\frac{\pi k_y y}{L_2}\right)\exp\left(i\frac{\pi k_z z}{L_3}\right). \tag{4}$$

Remark 1. Note that Eq. (4) is an infinite series. We truncate this series based on how well we want to approximate $\theta(\mathbf{r})$.

Since $\theta(\mathbf{r})$ is real and even, we have $a^*_{\mathbf{k}}=a_{-\mathbf{k}}$ and $a_{\mathbf{k}}$ is real. Now, we rescale x,y,z by π/L_1, π/L_2, and π/L_3, respectively, such that $-\pi \leq x,y,z \leq \pi$. Expressing $a_{\mathbf{k}}=A_{\mathbf{k}}/2$, we rewrite Eq. (4) as

$$\theta(\mathbf{r}) = \sum_{\mathbf{k}} A_{\mathbf{k}} \cos(\mathbf{k}\cdot\mathbf{r}). \tag{5}$$

We now show how to synthesize a space dependent rotation $\exp(\theta(\mathbf{r})Z)$, using nonselective rf pulses and linear 3D gradients. We define the unitary transformation,

$$U_{\mathbf{k}}(\beta) = \exp(\cos(\mathbf{k}\cdot\mathbf{r})X\beta), \tag{6}$$

and let

$$U_\theta = \prod_{\mathbf{k}} U_{\mathbf{k}}(A_{\mathbf{k}}). \tag{7}$$

Then, note

$$\exp\left(-\frac{\pi}{2}Y\right)U_\theta\exp\left(\frac{\pi}{2}Y\right) = \exp(\theta(\mathbf{r})Z), \tag{8}$$

the space dependent rotation we want to synthesize. We now show how to synthesize $U_{\mathbf{k}}(\beta)$. For small β,

$$U_{\mathbf{k}}(\beta) \approx \exp((\mathbf{k}\cdot\mathbf{r})Z)\exp\left(X\frac{\beta}{2}\right) \times\exp(-2(\mathbf{k}\cdot\mathbf{r})Z)\exp\left(X\frac{\beta}{2}\right)\exp((\mathbf{k}\cdot\mathbf{r})Z). \tag{9}$$

This just follows from the fact that

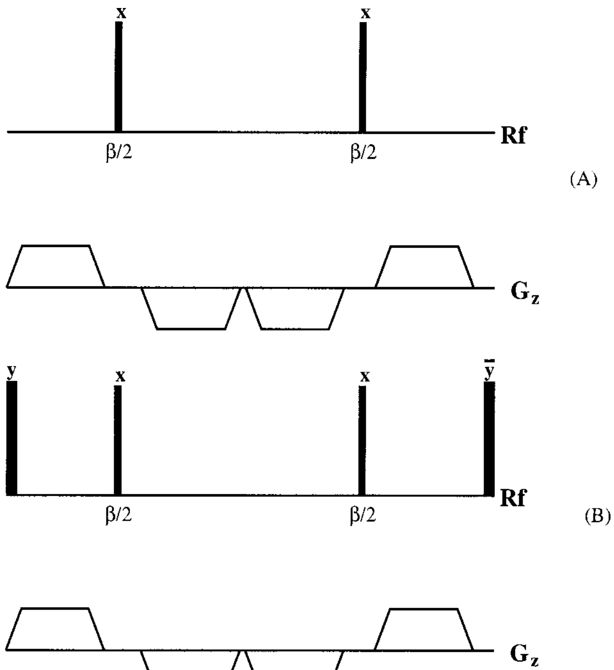

FIG. 2. (A) shows the pulse sequence element for implementing space dependent propagator $\exp(\beta\cos(kz)X)$. The spatial modulation is only in the z direction, so we only use gradients in the z direction. (B) shows the pulse sequence element for implementing space dependent propagator $\exp(\beta\cos(kz)Z)$ by the use of y and $\bar{y}$ pulses preceding and following the pulse element in (A).

$$\exp(\alpha Z)\exp\left(X\frac{\beta}{2}\right)\exp(-\alpha Z) = \exp\left((\cos(\alpha)X+\sin(\alpha)Y)\frac{\beta}{2}\right), \tag{10}$$

and for small β, we have

$$\exp\left((\cos(\alpha)X+\sin(\alpha)Y)\frac{\beta}{2}\right) \times\exp\left((\cos(\alpha)X-\sin(\alpha)Y)\frac{\beta}{2}\right) \approx \exp(\beta\cos(\alpha)X). \tag{11}$$

Let $n_{\mathbf{k}}$ be the smallest positive integer satisfying $A_{\mathbf{k}}=n_{\mathbf{k}}\beta$, such that $|\beta|<\beta_0$, and β_0 is chosen small enough so that approximation in Eq. (9) is valid. Then,

$$U_{\mathbf{k}}(A_{\mathbf{k}})=[U_{\mathbf{k}}(\beta)]^{n_{\mathbf{k}}}. \tag{12}$$

The evolution $\exp((\mathbf{k}\cdot\mathbf{r})Z)$ is obtained by turning the x,y,z gradients with strength k_xG_x, k_yG_y, and k_zG_z for τ units of time, such that

$$\gamma G_x\tau=1,\quad \gamma G_y\tau=1,\quad \gamma G_z\tau=1 \tag{13}$$

(the gradient strengths are in the terms of the new normalized coordinates). Note that we neglect terms of the form $\sigma\mathbf{G}$ in Eq. (1), as they are negligible.

For small β, Fig. 2(a) shows the building block for synthesizing the transformation $\exp(\beta\cos(kz)X)$, where a gradient of strength kG_z is turned on for time τ such that $\gamma G_z\tau=1$. This represents an X rotation on the spins such that the flip angle of the pulse is cosine modulated in the z direction. Synthesis of this space dependent rotation only requires gradients in the z direction.

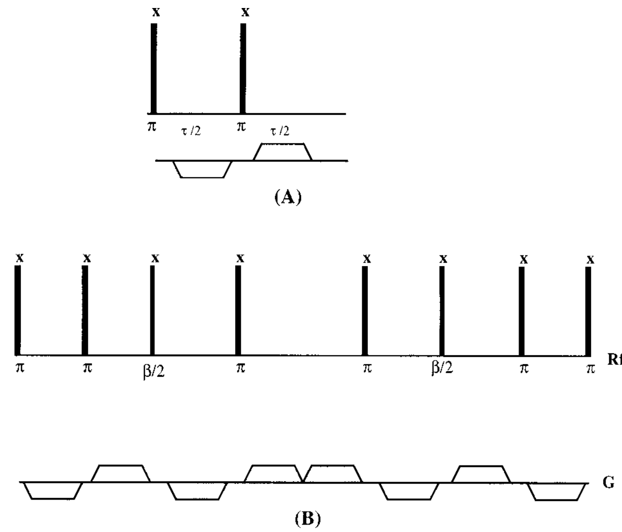

FIG. 3. (A) shows the pulse sequence element for refocusing the evolution of the phase due to the inhomogeneous magnetic field when the gradient is switched on. (B) shows the pulse sequence element for implementing space dependent propagator $\exp(\beta\cos(kz)X)$, which incorporates π pulses in (A), to refocus the evolution of phase due to inhomogeneous field. Inhomogeneity is assumed only in the z direction and therefore we only use one dimensional gradients here. The sequence in (B) when flanked by a y and $\bar{y}$ pulse will generate the rotation $\exp(\beta\cos(kz)Z)$ in the presence of an inhomogeneous field.

We have assumed that we can produce a space dependent rotation of the type $\exp((\mathbf{k}\cdot\mathbf{r})Z)$ by turning on the gradients $\mathbf{k}$ (k_x,k_y,k_z) for time τ. However, there is also an evolution of the phase of spins due to inhomogeneous fields. To refocus the phase that will evolve due to the inhomogeneous field, we apply a π pulse at the center of evolution at the time $\tau/2$ and reverse the direction of the gradients, i.e.,

$$\exp((\mathbf{k}\cdot\mathbf{r})Z)=\exp(-\pi X)\exp \times\left(\left(-\frac{\mathbf{k}\cdot\mathbf{r}}{2}+\Delta\phi(r)\right)Z\right)\exp(\pi X) \times\exp\left(\left(\frac{\mathbf{k}\cdot\mathbf{r}}{2}+\Delta\phi(r)\right)Z\right), \tag{14}$$

where $\Delta\phi(\mathbf{r})$ denotes the phase that arises at the location $\mathbf{r}$ due to inhomogeneous B_0 field in time $\tau/2$. The pulse element is shown in Fig. 3(a). The π pulse at time $\tau/2$, along with gradient switching, refocuses the phase $\Delta\phi(\mathbf{r})$ but keeps encoding due to the gradients being intact. Figure 3(b) shows the introduction of these refocusing π pulses in the middle of the pulse sequence in Fig. 2(a).

The complete algorithm for generating rf pulses and time varying gradients for producing the evolution $\exp(\phi_j(\mathbf{r})Z)$ can now be summarized as follows.

(1) Given $-\delta\phi(\mathbf{r})$, use Eq. (3) for finding (c_0,c_1,c_2,c_3) and computing $\theta(\mathbf{r})$.

(2) The coefficients $A_{\mathbf{k}}$ in Eq. (5) can now be computed as

$$\frac{A_{\mathbf{k}}}{2} = \frac{1}{(2\pi)^3}\int_{-\pi}^{\pi}\int_{-\pi}^{\pi}\int_{-\pi}^{\pi}\theta(\mathbf{r})\exp(i\mathbf{k}\cdot\mathbf{r})d^3r.$$

(3) Use Eqs. (9), (12), and (14) to synthesize $U_{\mathbf{k}}(A_{\mathbf{k}})$, and hence, $U=\Pi_{\mathbf{k}}U_{\mathbf{k}}(A_{\mathbf{k}})$.

(4) The desired compensating rotation

$$\exp(-\delta\phi(\mathbf{r})Z) = \exp\left(\frac{\pi}{2}Y\right)U_0U_\theta\exp\left(-\frac{\pi}{2}Y\right)U_1, \quad (15)$$

where c_0, $\mathbf{c}$ are as defined in Eq. (3) and $U_0 = \exp(c_0X)$, $U_G=\exp(-(\mathbf{c}\cdot\mathbf{r})Z)$ and U_θ are defined as in Eq. (7). The rotation U_G is obtained by simply turning on the gradient with appropriate strength and duration. The rotation U_0 is obtained by application of rf pulse.

If the inhomogeneous field distribution is known, then we can use the procedure described above to compute parameters of the rotations U_0, U_G, and U_θ. The inhomogeneous field distribution can be mapped by field mapping methods.[9] The field mapping techniques are routinely used in the gradient shimming procedures on commercial spectrometers to adjust the current in the shim coils.[10]

The main point of this paper is that an explicit mapping of the field and the resulting computational procedure described above need not be carried out explicitly. We show how to design experiments, which help us to learn the function $\delta B(\mathbf{r})$, by directly learning the parameters of the rotations U_0, U_G, and U_θ that will correct for the function $\delta B(r)$. This is done by a sequence of parameter optimizations that progressively work on narrowing the linewidth of the resonance. The main advantage of this technique is that it avoids calibrating the relationship between space dependent rotations and the parameters of the pulse and the gradient waveforms. The appropriate parameters of the pulse and gradient waveforms can be directly learned by a sequence of parameter optimizations as described below.

To fix the main ideas of this paper, we for now fix the chemical shift σ to a specified value σ_0 (in practice, this means analyzing a well isolated resonance line) and consider the Bloch equation in a frame rotating around the z axis with frequency $\omega_0=\gamma B_0(1-\sigma_0)$. We obtain that in a frame rotating around the z axis with frequency ω_0, we get that the free induction signal from the whole sample is

$$s(t) = \int_{-\infty}^{\infty} S(\omega)\exp(-j\omega t),$$

where ω is the deviation from the nominal frequency ω_0. Then, observe that $|S(\omega)|$ is the absolute value of Fourier transform of this signal $s(t)$ and the spread or the width of the spectrum is simply

$$\int_{-\infty}^{\infty}\omega^2|S(\omega)|d\omega.$$

However, note that for constant C,

$$\int_{-\infty}^{\infty}\omega^2|S(\omega)|d\omega = C\int_0^{L_3}\int_0^{L_2}\int_0^{L_1}\omega^2(\mathbf{r})d^3r. \quad (16)$$

Now, we expand the phase $\delta\phi(\mathbf{r})$, in Eq. (2), in terms of suitable orthogonal basis (we remark on the choice of orthogonal basis subsequently), i.e.,

$$\delta\phi(\mathbf{r}) = \sum_{j=1}^{\infty} a_j\phi_j(\mathbf{r}), \quad (17)$$

where

$$\langle\phi_i,\phi_j\rangle = \int_0^{L_3}\int_0^{L_2}\int_0^{L_1}\phi_i(x,y,z)\phi_j(x,y,z)dxdydz = \delta_{ij},$$

where $\delta_{ij}=0$ for $i\neq j$ and 1 for $i=j$.

If $\delta\phi(\mathbf{r})$ is known, then a_j can be computed. Since we do not know $\delta\phi(\mathbf{r})$, we aim to estimate the unknown field profile $\delta\phi(\mathbf{r})$ by estimating a_j. We start by making a guess at a_j and synthesize a space dependent rotation $\exp(-a_1\phi_1(\mathbf{r})Z)$ in Fig. 1. The application of space dependent rotation followed by free precession for time T as in Fig. 1 results in an effective phase evolution $\exp([\delta\phi(\mathbf{r})-a_1\phi_1(\mathbf{r})]Z)$, and an effective spatial distribution of Larmor frequencies given by

$$\omega(\mathbf{r}) - a_1\omega_1(\mathbf{r}) = C\frac{\delta\phi(\mathbf{r}) - a_1\phi_1(\mathbf{r})}{T}.$$

The width of the resulting resonance line in the spectrum is given by

$$\int_0^{L_3}\int_0^{L_2}\int_0^{L_1}(\omega(\mathbf{r}) - a_1\omega_1(\mathbf{r}))^2d^3r. \quad (18)$$

Now, we can begin to scan the parameter a_1 and monitor the width of the resonance. The function in Eq. (18) is a quadratic function of a_1 and has a unique minimum. We first locate whether increasing (or decreasing) a_1 reduces the linewidth, and if so, we keep increasing (or decreasing) a_1, until the linewidth begins to increase again. This gives the optimal value a_1^* of a_1. We can use a similar procedure to determine a_j^* for $j=1,\ldots,N$, where N is chosen sufficiently large. We continue this process inductively by first computing the optimal values of a_j^* for $j=1,\ldots,N$ and then synthesizing

$$\exp\left(-\sum_{j=1}^{N}a_j^*\phi_j(\mathbf{r}) - a_{N+1}\phi_{N+1}(\mathbf{r})Z\right),$$

where the parameter a_{N+1} is scanned to get the optimal value. The process is continued, until the resonance line is sufficiently narrow. In this case, we claim, we know the distribution of the inhomogeneous field to desired level of confidence.

Remark 2. It is important to note that we do not simultaneously vary the parameters a_j. This would make the search impractical for real time applications. The optimal value of the parameters a_j can be determined sequentially, which is an attractive feature of the proposed method. The optimal value a_j^* is simply $\langle\delta\phi(\mathbf{r}),\phi_j(\mathbf{r})\rangle$. Since $\delta\phi(\mathbf{r})$, is not known, we obtain a_j^* by the methods described.

Remark 3. There are various possible choices of the basis function $\phi_j(\mathbf{r})$. The choice of ϕ_j should be made so that one would require a minimum number of basis functions to represent the spatially inhomogeneous field. This would then require some *a priori* statistical knowledge of the field distribution. We have shown how to synthesize a space dependent rotation $\exp(\phi(\mathbf{r})Z)$. The synthesis process itself suggests one possible choice of basis set in three dimensions, the Fourier basis, which we use in our experiment.

Remark 4. Once the coefficients a_j in Eq. (17) are known, we can now perform the experiment depicted in Fig. 1 with the space dependent transformation

$$U(r) = \exp\left(-\sum_j a_j\phi_j(\mathbf{r})\right).$$

This rotation then compensates the phase acquired by spins due to precession in inhomogeneous field $\delta B(\mathbf{r})$ for time T. This then helps us obtain high resolution spectrum.

III. EXPERIMENTAL

The Fourier synthesis methods for obtaining resolved spectra in inhomogeneous fields are demonstrated on a 500 MHz Bruker Magnet using a sample consisting of DSS (2,2-dimethyl-2-silapentane-5-sulfonic acid) and DFTMP (difluoro-trimethlysilanyl-methyl phosphonic acid) with two closely placed, 0.2 ppm apart, resonances as shown in Fig. 7(D). The B_0 field inhomogeneities are introduced in a controlled fashion by changing the settings of the shim coils from their nominal value. The basic pulse sequence used for compensating the field inhomogeneities is the same as in the Fig. 1. The compensating U block consisting of gradients and rf pulses is followed by a delay for time T during which the chemical shift of the spins evolve followed by acquisition of a complex point. The time T is dictated by the spectral width (SW) and corresponds to the usual dwell time during free induction decay (FID) acquisition, i.e., $T=1/\mathrm{SW}$. In our experiments, SW of 8 ppm corresponding to a dwell time of 125 μs was chosen, where the number of acquired points were 2 K.

The magnet was deshimmed by changing the nominal values of z and z^2 shim settings, which introduce inhomogeneous fields that have z and z^2 dependences. The U block used in this experiment in Fig. 1 is depicted in Fig. 4. The inhomogeneous z field can be compensated by simply introducing a gradient G_1 in Fig. 4, of suitable strength. The exact strength or duration of the gradient depends on the z variation of static B_0 field inhomogeneity and is calibrated by a sequence of experiments as described in the main text, where the goal is progressive narrowing of the resonance line.

To offset the z^2 inhomogeneity in the static field, we synthesize a space dependent rotation $\exp(\beta\cos(k_z z)Z)$, as described in Sec. II of the main text. The pulse sequence for generating this transformation is described in Figs. 2(b) and 3(b). Assuming that the z dimension of the sample is normalized between $[-\pi,\pi]$, such that $k_z \ll 1$, we have

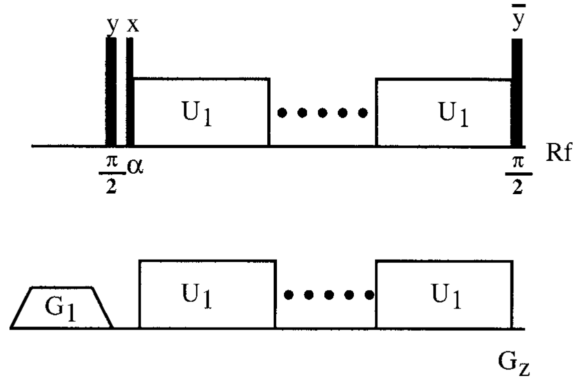

FIG. 4. The pulse sequence in our experiment that comprises the U block in Fig. 2. The U_1 block in the above figure is as shown in Fig. 3(b). Repeated applications of the Block U_1 are used to synthesize U_θ in Eq. (15). The gradient G_1 synthesizes the U_G rotation in Eq. (15). The x-phase pulse with flip angle α synthesizes U_0 in Eq. (15). The flip angle β in the U_1 block, the flip angle α, and the strength of the gradient G_1 are all optimized.

$$\cos(k_z z) \sim 1 - \frac{(k_z z)^2}{2}. \tag{19}$$

Therefore, by the appropriate choice of β, in $\exp(\beta\cos(k_z z)Z)$, a rotation of the form $\exp((a-bz^2)Z)$ is synthesized, which compensates for z^2 inhomogeneity. In order to achieve small value of k_z, we first calibrate our gradients such that $k_z=1$. This is achieved by synthesizing a space dependent rotation of the form $\exp(\pi/2\cos(k_z z)X)$, as shown in Fig. 2(a), in a shimmed magnet and observing the FID in the presence of a gradient. The resulting spectra shows a frequency (that encodes space) dependent excitation. Figure 5 shows the typical spectra, where the number of cycles in the spectra simply represent the value of k_z. This helps to calibrate the gradient strength that will produce a desired k_z. We now reduce the gradient strength or duration sufficiently such that $k_z \ll 1$ and the approximation in Eq. (19) holds. In our experiments, the gradients in Fig. 3(b) were operated at 5% of their maximum value, where this maximum value cor-

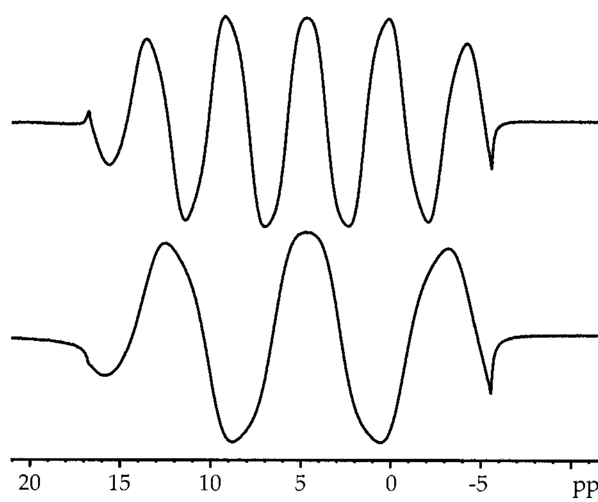

FIG. 5. The space dependent cosine modulated excitation produced by pulse sequence in Fig. 2(a), followed by acquisition in the presence of a gradient. This helps to calibrate the strength of the gradients. By increasing the strength of the gradient in Fig. 2(a), the frequency of the modulation can be increased, as shown in the top spectra when compared to the bottom spectra.

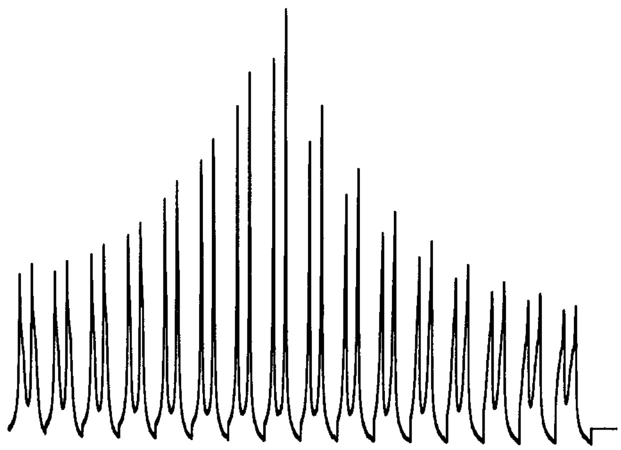

FIG. 6. A series of spectra generated, as described in Fig. 1, as a result of optimization over the choice of flip angle β in the U_1 block in Fig. 4.

responds to 0.5 T/m. The time of a rectangular gradient pulse in Fig. 3(b) was chosen as 20 μs. The gradient recovery time in our experiments was 100 μs. This is the dead time after the gradient is switched off before an rf pulse can be applied.

Now, by doing a parameter optimization over an angle β, we can find the optimal value of β. The result of this optimization is depicted in Fig. 6. The constant a in $\exp((a-bz^2)Z)$ produces a uniform shift in all the frequencies. This can simply be corrected by a constant Z rotation of the form $\exp(-\alpha Z)$ by changing the flip angle α in Fig. 4. The complete compensating block to offset inhomogeneity is shown in Fig. 4. The pulse sequence block synthesizing $\exp(\beta \cos(k_z z)Z)$ assumes a small flip angle β. Larger values of β are achieved by repeated application of such blocks, as shown in 4. In our experiment the block was repeated twice. Figure 7(c) shows the spectra in a field with z^1 and z^2 inhomogeneities. Figure 7(b) shows the spectra after it is corrected by application of a compensating block. Figure 7(a) shows how the uniform shift in the frequencies can be corrected by a suitable flip angle α in Fig. 4.

To compare how well this method performs, a reference spectrum in shimmed magnet is collected, as shown in Fig. 7(d). The spectrum is obtained by using a pulse sequence, as in Fig. 1, where the U block now consists of free evolution for time τ and a refocusing pulse at the center. The time τ is chosen exactly the same as is required to synthesize the U block in the main experiment. Therefore, there is no evolution during the U block except relaxation. This ensures that relaxation effects in both experiments, one in homogeneous field and another in inhomogeneous field, are the same. The match between Figs. 7(a) and 7(d) is quite good.

IV. DISCUSSION

The proposed technique is discussed and demonstrated for an ensemble of noninteracting spins $\frac{1}{2}$. Extension to spin systems with coupled heteronuclear spins is relatively straightforward. The refocusing π pulses on spin I in Fig. 2(a) will also refocus the heteronuclear couplings to another spin S. As a result, there is no heteronuclear coupling evolution of the spins during the synthesis of U block in Fig. 1.

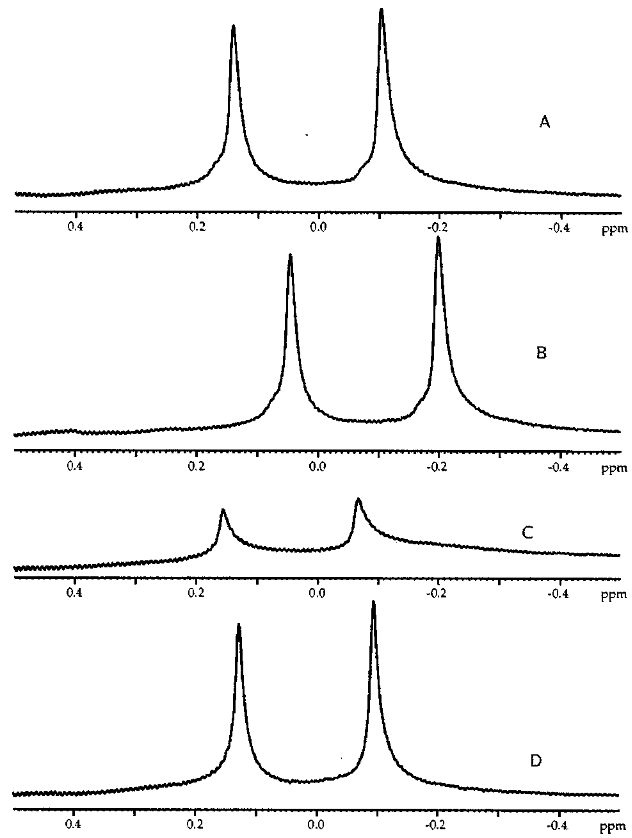

FIG. 7. (D) shows the spectra of DSS and DFTMP in a shimmed magnet. The linewidths of the resonance at −0.1 and 0.1 ppm are measured to be 8.78 and 8.3 Hz, respectively, in a shimmed field in (D). (C) shows the spectra when the magnet is deshimmed by changing the setting of z^1 shims by 3000 units from their nominal value (corresponding to introducing a linear inhomogeneous field) and by changing the setting of the z^2 shims (corresponding to introducing a quadratic inhomogeneous field), by 3000 units from their nominal value. (B) shows the spectra after it is corrected by application of a compensating block in Fig. 2. The frequency shift in the spectra arises from the constant a in Eq. (19), which can be offset by a constant Z rotation, as shown in (A). The linewidths of resonances at −0.1 and 0.1 ppm for the spectra in (A) are 10.25 and 9.27 Hz, respectively.

However, couplings between homonuclear spins are not refocused, as the π pulses are not selective. In principle, it seems possible to engineer a pulse sequence consisting of selective rotations that will refocus couplings between homonuclear spins during the synthesis of a space dependent rotation. However, this would require *a priori* chemical shift information of the homonuclear spins. Further methodology development is required to find efficient methods to refocus homonuclear couplings without *a priori* knowledge of the chemical shifts in Fig. 1. We plan to pursue this in our future work.

Most of the time spent in executing the compensating pulse sequence in Fig. 1 is required in the synthesis of the U Block. This, in turn, depends on the strength of the gradients and the time allowed for gradient recovery. This time also determines the relaxation losses in the system. In our experiment, the synthesis of U block required 3.8 ms of which 3.2 ms was simply gradient recovery time. Clearly, it is possible to significantly reduce this time. In a dedicated system custom designed for spectroscopy in inhomogeneous field, strong gradients with low recovery time are desirable.

The proposed methodology assumes that $|\delta B(r)|$, the inhomogeneities in the static field, are small compared to $B_{\rm rf}^{\rm max}$, the maximum available rf power, and a hard π pulse as in Fig. 2(a) on the spins will refocus the chemical shift evolution in inhomogeneous field as in Fig. 1. Assuming a moderately high rf power of 50 kHz on protons, this would limit $|\delta B(r)| \leq 10^{-3} T$, over the sample of proton spins. This limitation on the B_0 inhomogeneities can be alleviated to some extent by use of adiabatic refocusing pulses in Fig. 1. This would come at the cost of increased time to produce the space dependent rotations and therefore increased relaxation losses. Nevertheless, it appears that the present methodology would still be limited for large B_0 field inhomogeneities $|\delta B(r)| \sim 10 B_{\rm rf}^{\rm max}$. For larger field inhomogeneities, it may be possible to use selective excitations of the sample over which inhomogeneities are comparable to the strength of rf fields. In future work, we plan to address these issues in the context of a low-field system.

The ability to engineer space dependent rotations is also expected to have applications in magnetic resonance imaging. By engineering phase encodings with nonlinear space dependence, simultaneous encoding of two space dimensions may be possible. This would significantly reduce the imaging time compared to state-of-the-art imaging sequences which use separate phase encodings for independent dimensions.

V. CONCLUSION

In this paper, we showed that it is possible to learn the profile of inhomogeneous magnetic field with the help of rf pulses and time varying gradients. We have shown how to design a sequence of experiments that progressively work on narrowing the resonance line of the spectra obtained from spin precession in inhomogeneous fields. Reducing the linewidth below a certain limit is the equivalent to learning the field profile with a desired confidence. Once the field inhomogeneity is mapped out, it is possible to impart the transverse magnetization of spins a desired phase as a function of the spatial (x, y, z) location (to desired level of accuracy).[1] Therefore, it is possible to precompensate the phase that will be acquired by spins at different spatial locations due to inhomogeneous magnetic fields. With this precompensation, the chemical shift information of the spins can be reliably extracted and high resolution NMR spectrum can be obtained. It is expected that methods presented here will have applications in NMR spectroscopy and imaging in inhomogeneous fields.

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