Fourier decompositions and pulse sequence design algorithms for nuclear magnetic resonance in inhomogeneous fields

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In this paper, we introduce algorithms based on Fourier synthesis for designing phase compensating rf pulse sequences for high-resolution nuclear magnetic resonance (NMR) spectroscopy in an inhomogeneous B_0 field. We show that using radio frequency pulses and time varying linear gradients in three dimensions, it is possible to impart the transverse magnetization of spins phase, which is a desired function of the spatial (x,y,z) location. Such a sequence can be used 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.
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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 volumes. This usually comes at the cost both in price of NMR systems and in size demanded by NMR magnets. Such homogeneities are not achievable when dealing with spatially heterogeneous tissues or employing remote NMR arrangements. A number of methods have recently been proposed to compensate for the B_0 inhomogeneity using radio frequency fields.[1–7] These either use an inhomogeneous rf field matched to the inhomogeneity of the B_0 field[4] or use field gradients along with radio frequency pulses to compensate for the phase that will be accumulated due to inhomogeneous B_0 magnetic field in one dimension.[7] In this paper, we show that arbitrary phase compensation as a function of three dimensional spatial position is possible using spatially nonselective radio frequency pulse sequence and linear time varying three dimensional (3D) gradients. We provide explicit rf pulse sequences and time varying gradients for synthesizing any desired phase as a function of the spatial location. These sequences are derived using methods of Fourier synthesis. If the spatial dependence of the field inhomogeneities can be mapped out *a priori*, then the phase accumulation due to these inhomogeneities can be precompensated and high resolution spectra can be obtained.

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 three dimensional time varying gradient vector and (X, Y, Z) represents generators of rotations around x, y, z axes and $B_x(t) = B_{\rm rf}(t)\cos(\omega_0 t+\psi(t))$ and $B_y(t)=B_{\rm rf}(t)\sin(\omega_0 t+\psi(t))$ represents the x and y components of the rf field. 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 $B_{\rm rf}(t)$ and $\psi(t)$ are the amplitude and phase of the rf field. Here $\delta B(\mathbf{r})$ is the inhomogeneity of the B_0 field at spatial location $\mathbf{r}$. In the absence of rf fields and gradients, the spins precessing at the location $\mathbf{r}=(x,y,z)$ will accumulate in time t, a phase evolution

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

where $\delta B(\mathbf{r})$ is the inhomogeneity of the B_0 field at spatial location $\mathbf{r}$. Then assuming $\delta B(r) \ll B_0$, and that the chemical shift σ is only parts per million, we can neglect the term $\sigma\gamma\delta B(\mathbf{r})t$ and write $\phi(\mathbf{r})=\gamma B_0(1-\sigma)t+\underbrace{\gamma\delta B(\mathbf{r})t}_{\delta\phi(\mathbf{r})}$. We also assume that the strength of the maximum rf field $B_{\rm rf} \gg \delta B(\mathbf{r})$. 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 use of broadband excitation rf pulses. To get the main ideas of the paper across we will stick to this assumption. Rewriting Bloch equation in a frame rotating around z axis with frequency ω_0, we get

$$\frac{dM(\mathbf{r})}{dt} = \gamma\{(-\sigma B_0+(1-\sigma)(\delta B(\mathbf{r})+\mathbf{G}(t)\cdot\mathbf{r}))Z+u(t)X + v(t)Y\}M(\mathbf{r}), \quad (2)$$

where $(u(t),v(t))=B_{\rm rf}(t)(\cos\psi(t),\sin\psi(t))$.

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We now need to compensate for the position dependent phase $\delta\phi(\mathbf{r})$ using radio frequency pulses and time varying gradients. We show how to synthesize a space dependent rotation $\exp(-\delta\phi(\mathbf{r})Z)$ with the help of rf pulses and linear time-varying gradients. This rotation acting on the initial Bloch vector $(M_x(\mathbf{r}),M_y(\mathbf{r}),M_z(\mathbf{r}))=(1,0,0)$ will precompensate for the phase accumulated due to inhomogeneity in the B_0 field. This precompensation then helps to acquire high resolution spectrum.

Given arbitrary phase $\delta\phi(x,y,z)$, for $0<x<L_1$ and $0<y<L_2$ and $0<z<L_3$, we can first extract from it a constant and linearly varying 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 square 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 $\langle\phi_1,\phi_2\rangle$ simply denotes the integral $\int_0^{L_3}\int_0^{L_2}\int_0^{L_1}\phi_1(x,y,z)\phi_2(x,y,z)dxdydz$. 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 $\theta(L_1+x,\ldots,\ldots)=\theta(L_1-x,\ldots,\ldots)$ for $0<x<L_1$. Similarly for y and z. Note $\theta(x,y,z)$ is now defined on $0<x<2L_1$ and $0<y<2L_2$ and $0<z<2L_3$ and can be expanded as

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

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, we have $a_{\mathbf{k}}^*=a_{-\mathbf{k}}$. Now we rescale x,y,z by π/L_1, π/L_2, and π/L_3, respectively, such that $0\leqslant x,y,z\leqslant 2\pi$. Expressing $a_{\mathbf{k}}=(A_{\mathbf{k}}/2)\exp(i\gamma_k)$, we rewrite Eq. (4) as

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

where $A_{\mathbf{k}}\geqslant 0$ and $0\leqslant\gamma_{\mathbf{k}}\leqslant 2\pi$.

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

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

where β is a small flip angle as described below, and let

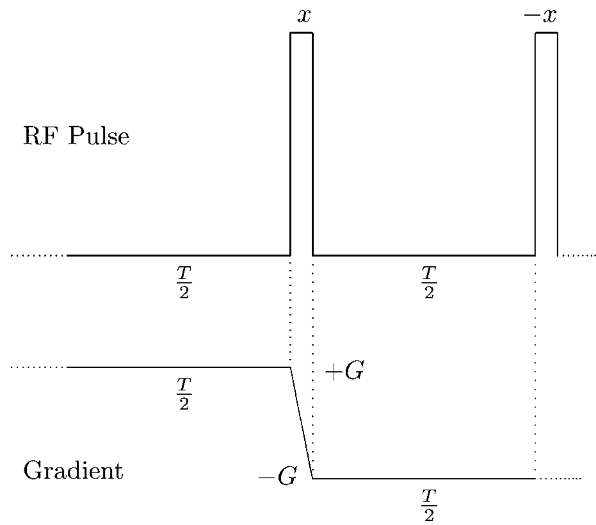

FIG. 1. The pulse sequence element for implementing space dependent propagator in Eq. (15). The hard rf pulses are π pulses. We just show one dimensional gradients here.

$$U = \prod_{\mathbf{k}} U_{\mathbf{k},\gamma_{\mathbf{k}}}(A_{\mathbf{k}}). \tag{7}$$

Then note

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

the space dependent rotation we want to synthesize.

We now show how to synthesize $U_{\mathbf{k},\alpha}(\beta)$. For small β,

$$\begin{aligned} U_{\mathbf{k},\alpha}(\beta) &\approx \exp((\mathbf{k}\cdot\mathbf{r}+\alpha)Z) \\ &\quad\times\exp\left(X\frac{\beta}{2}\right)\exp(-2(\mathbf{k}\cdot\mathbf{r}+\alpha)Z) \\ &\quad\times\exp\left(X\frac{\beta}{2}\right)\exp((\mathbf{k}\cdot\mathbf{r}+\alpha)Z). \end{aligned} \tag{9}$$

This just follows from the fact that

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

and for small β, we have

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

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

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

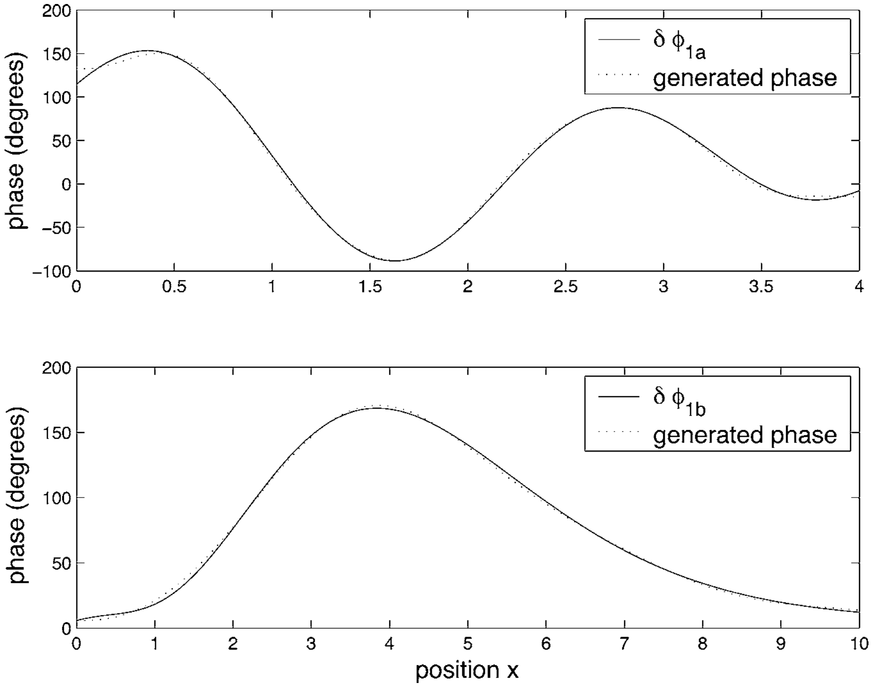

FIG. 2. (Top panel) A comparison of the one dimensional phase $\delta\phi_{1a}$ in Eq. (16) that we desire to compensate (shown in solid) and of the actual compensation provided by the pulse sequence while keeping nine Fourier components (shown in dotted). The bottom panel shows a comparison of the one dimensional phase $\delta\phi_{1b}$ in Eq. (17) that we desire to compensate (shown in solid) and of the actual compensation provided by the pulse sequence while keeping six Fourier components (shown in dotted).

We now only need to show how to synthesize $\exp((\mathbf{k}\cdot\mathbf{r}+\alpha)Z)$. Note this rotation can be decomposed as $\exp((\mathbf{k}\cdot\mathbf{r})Z)\exp(\alpha Z)$. The evolution $\exp(\alpha Z)$ can be obtained by rf pulses, i.e.,

$$\exp(\alpha Z)=\exp\left(\frac{\pi}{2}X\right)\exp(\alpha Y)\exp\left(-\frac{\pi}{2}X\right). \tag{13}$$

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 T units of time, such that

$$\gamma G_xT=1, \quad \gamma G_yT=1, \quad \gamma G_zT=1 \tag{14}$$

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

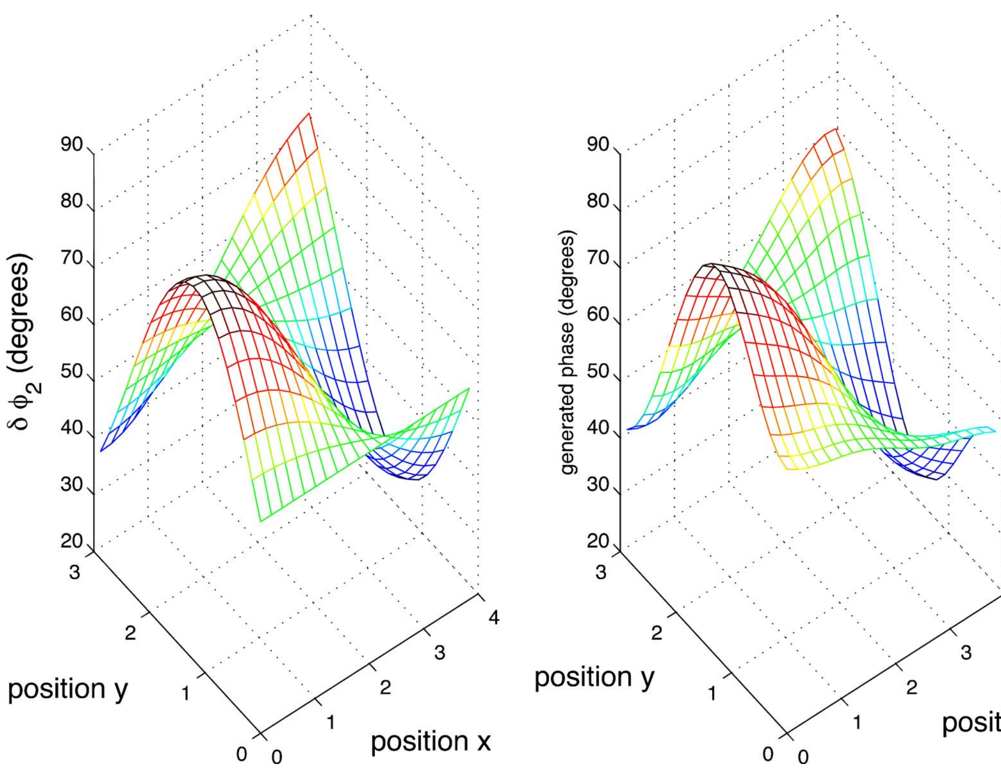

FIG. 3. A comparison of the two dimensional phase $\delta\phi_2$ we wish to compensate (shown on left) and of the actual compensation provided by the pulse sequence (shown on right) while keeping all admissible Fourier pairs (k_x,k_y), satisfying $k_x^2+k_y^2\leq 10$. The mean of the absolute value of phase error is 1.25° and the maximum error is 9°.

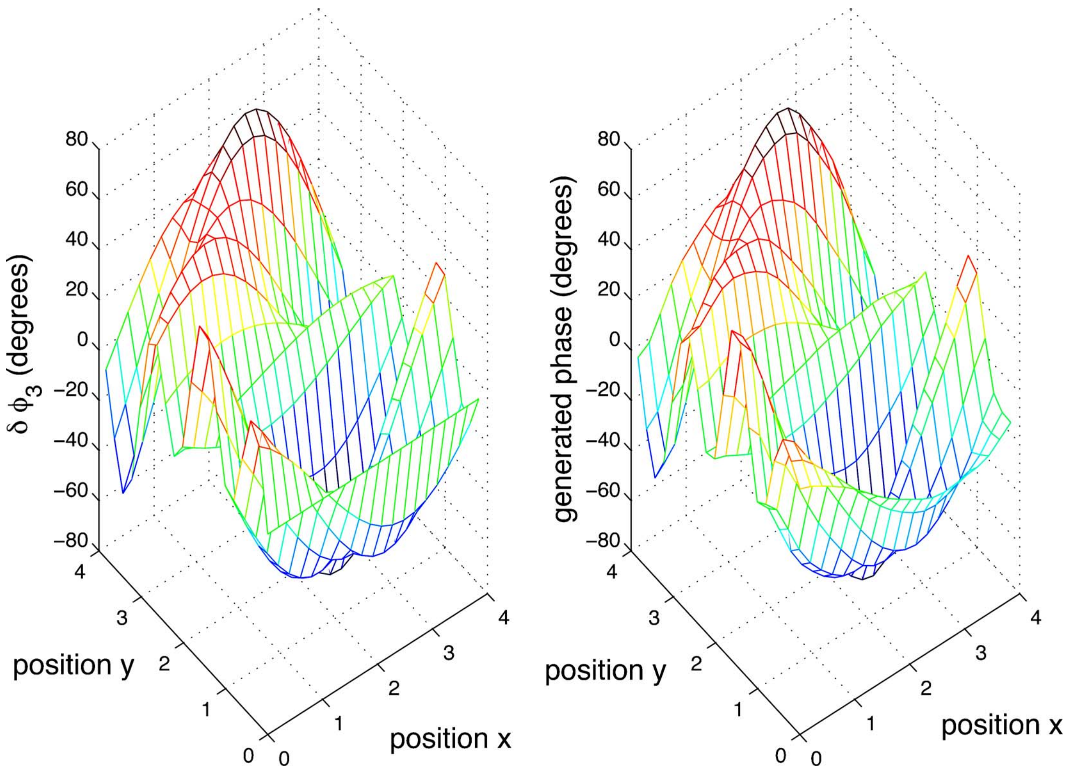

FIG. 4. A comparison of the two dimensional phase $\delta\phi_3$ we wish to compensate (shown on left) and of the actual compensation provided by the pulse sequence, when we retain all the Fourier pairs (k_x,k_y) satisfying $k_x^2+k_y^2\leq k^2$, where k^2 is chosen to be 100 (shown on right). The mean of the absolute value of phase error is 2.4° and the maximum error is 10°.

Eq. (2) as they are negligible. To refocus the phase that will evolve due to the inhomogeneous field, we apply a π pulse in the center of evolution at the time $T/2$ and reverse the direction of the gradients, i.e.,

$$\exp((\mathbf{k}\cdot\mathbf{r})Z)=\exp(-\pi X)\exp\left(\left(-\frac{\mathbf{k}\cdot\mathbf{r}}{2}+\Delta\phi(\mathbf{r})\right)Z\right)\times\exp(\pi X)\exp\left(\left(\frac{\mathbf{k}\cdot\mathbf{r}}{2}+\Delta\phi(\mathbf{r})\right)Z\right), \quad (15)$$

where $\Delta\phi(\mathbf{r})$ denotes the phase that arises at the location $\mathbf{r}$ due to inhomogeneous B_0 field in time $T/2$. The pulse element is shown in Fig. 1. The π pulse at time $T/2$, along with gradient switching, refocuses the phase $\Delta\phi(\mathbf{r})$, but keeps encoding due to the gradients intact.

The complete algorithm for generating rf pulses and time varying gradients for producing the evolution $\exp(-\delta\phi(\mathbf{r})Z)$ 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 $A_{\mathbf{k}}$ and $\gamma_{\mathbf{k}}$ in Eq. (5) can now be computed as

$$\frac{A_{\mathbf{k}}}{2}\exp(i\gamma_{\mathbf{k}})=\frac{1}{(2\pi)^3}\int_0^{2\pi}\int_0^{2\pi}\int_0^{2\pi}\theta(\mathbf{r})\exp(i\mathbf{k}\cdot\mathbf{r})d^3r.$$

(3) Use Eqs. (9), (12), and (15) to synthesize $U_{\mathbf{k},\gamma_{\mathbf{k}}}(A_{\mathbf{k}})$ and hence $U=\Pi_{\mathbf{k}}U_{\mathbf{k},\gamma_{\mathbf{k}}}(A_{\mathbf{k}})$.

(4) The desired compensating rotation

$$\exp(-\delta\phi(\mathbf{r})Z)=\exp\left(\frac{\pi}{2}Y\right)\exp(c_0X)U\times\exp\left(-\frac{\pi}{2}Y\right)\exp(-(\mathbf{c}\cdot\mathbf{r})Z),$$

where $c_0,\mathbf{c}$ are as defined in Eq. (3).

We have demonstrated a constructive way of synthesizing an arbitrary space dependent transformation $\exp(\theta(\mathbf{r})Z)$ using time varying linear gradients and rf pulses. Similar constructions can be used to produce arbitrary space dependent rotation $\Theta(\mathbf{r})$. We just need to observe that we an use Euler angle decomposition to write

$$\Theta(\mathbf{r})=\exp(\theta_1(\mathbf{r})X)\exp(\theta_2(\mathbf{r})Z)\exp(\theta_3(\mathbf{r})X).$$

Each of the term on the right hand side (RHS) of the above equation can now be synthesized using constructions detailed in the paper.

The time for the synthesis of space dependent rotations $\exp((\mathbf{k}\cdot\mathbf{r})Z)$ in Eq. (15) depends on the strength of the gradients and dictates the time of the overall pulse sequence. Therefore the time for implementing the phase compensating pulse sequences is determined by the strength of the gradients and number of terms in the Fourier approximation.

III. SIMULATIONS

In this section, we provide simulation results on phase compensation obtained by use of nonselective rf pulses and time varying gradients obtained using the algorithm provided

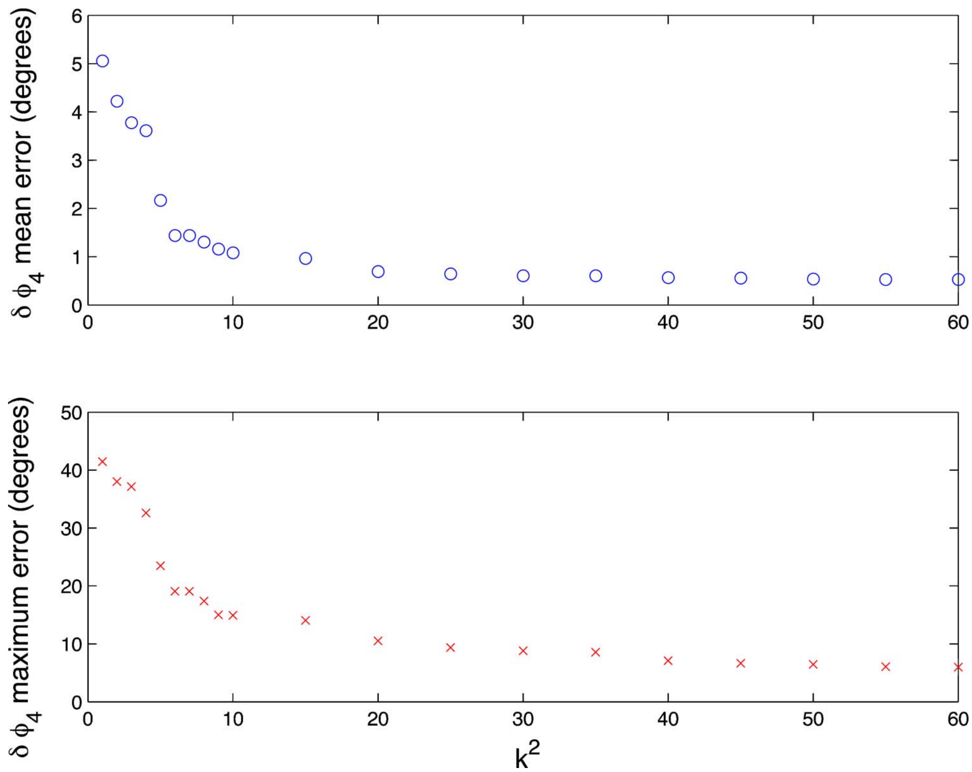

FIG. 5. The mean (top curve) and the maximum error (bottom curve) obtained in approximating the function ϕ_4 as a function of k^2. As before, we retain all the admissible Fourier triplets (k_x,k_y,k_z), satisfying $k_x^2+k_y^2+k_z^2 \leqslant k^2$. We see that both the mean and the maximum phase error (over all spatial positions) decreases with the inclusion of more Fourier components (larger values of k).

in this paper. All simulations were done using MATLAB. Simulations assumed the ratio of maximum rf power to maximum inhomogeneity of 25:1, corresponding to an inhomogeneity of ±2 kHz with rf power of 50 kHz. In simulations, the value of the small flip angle β_0 used in Eq. (6) is 10°. For the first example, consider a phase dispersion in one dimension,

$$\delta\phi_{1a}(x) = 0.3x + \cos(x) + \cos(2x) + \sin(3x), \tag{16}$$

where $0 \leqslant x \leqslant 4$. The spatial units are left unspecified as gradient strength is specified per spatial unit and this in Eq. (14) determines the time T to implement the propagator in Eq. (15). In practice, a spatial extent of 10 mm and a gradient strength G of 100 mT/m would correspond to an approximate time $T \approx 10$ μs in Eq. (14). Figure 2 displays the results of simulation. In this example, we retain first nine terms in the Fourier series in Eq. (4). The maximum error occurs near the boundaries, but this error can be made arbitrarily small by increasing the number of terms in the Fourier expansion.

As a second example, again consider the one dimensional phase profile

$$\delta\phi_{1b}(x) = 0.1 + (0.3x + 0.5x^5)e^{-1.3x}, \tag{17}$$

where $0 \leqslant x \leqslant 10$. Figure 2 again displays the results of the compensation algorithm. In this case we retain first six Fourier components.

As a third example, consider a two dimensional phase profile, where the phase we want to compensate is

$$\delta\phi_2(x,y) = 1 + 0.5\sin(x)\cos(y), \tag{18}$$

where $0 \leqslant x \leqslant 4$ and $0 \leqslant y \leqslant 3$. In this example, we retain all the Fourier pairs (k_x,k_y) satisfying $k_x^2+k_y^2 \leqslant k^2$, where k^2 is chosen to be 10. The results are displayed in Fig. 3.

As a fourth example, we consider the phase profile

$$\delta\phi_3(x,y) = \cos(2x)\cos(y)\sin(\pi x) - \sin(\sqrt{2}x)\sin(y) \tag{19}$$

using the pulse design algorithm over the region $0 \leqslant x \leqslant 4$ and $0 \leqslant y \leqslant 4$. In this example, we retain all the Fourier pairs (k_x,k_y) satisfying $k_x^2+k_y^2 \leqslant k^2$, where k^2 is chosen to be 100. Figure 4 shows the results. By keeping more terms in the Fourier expansion for the relatively complex phase profile $\delta\phi_3$, the error in Fig. 4 can be made as small as desired.

Finally we consider B_0 inhomogeneity in 3-dimensional volume. We consider a 3D phase profile of

$$\delta\phi_4(x,y,z) = z\sin(x)y^2, \tag{20}$$

where $0 \leqslant x \leqslant 4$, $0 \leqslant y \leqslant 1$, and $0 \leqslant z \leqslant 1$. In Fig. 5, we plot the mean of the absolute value of error (top curve) and the maximum error (bottom curve) obtained in approximating the given profile as a function of k^2. As before, we retain all the admissible Fourier triplets (k_x,k_y,k_z), satisfying $k_x^2+k_y^2+k_z^2 \leqslant k^2$. We see that both the mean and maximum phase errors (computed over all spatial positions) decrease with the inclusion of more Fourier components.

IV. CONCLUSION

In this paper we showed that arbitrary phase compensation as a function of three dimensional spatial position is possible using radio frequency pulse sequence and 3D gradients. We provided explicit pulse sequences that impart the transverse magnetization of spins a desired phase as a function of the spatial (x, y, z) location (to desired level of accuracy). Our construction of the pulse sequences may not be the shortest (in terms of time). Finding the shortest sequence of time varying gradients and radio frequency pulses to produce a desired spatial phase is important as it will minimize the relaxation effects that are always present and have been neglected in our treatment here. This is a problem in optimal control.[8] In Eq. (2) we can treat $(\mathbf{G}(t), u(t), v(t))$ as controls and $\mathbf{r}$ as parameters. The goal is to find $(\mathbf{G}(t), u(t), v(t))$, that will effect the rotation $\exp(-\delta\phi(\mathbf{r})Z)$ in minimum time. We plan to address this in our future work. It is expected that methods presented here will have wide applications in NMR spectroscopy and imaging in inhomogeneous fields.

ACKNOWLEDGMENTS

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