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# Imaging sequences for hyperpolarized solids

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**Abstract:** Hyperpolarization is one of the approaches to enhance Nuclear Magnetic Resonance (NMR) and Magnetic Resonance Imaging (MRI) signal by increasing the population difference between the nuclear spin states. Imaging hyperpolarized solids opens up extensive possibilities, yet is challenging to perform. The highly populated state is normally not replenishable to the initial polarization level by spin-lattice relaxation, which regular MRI sequences rely on. This makes it necessary to carefully “budget” the polarization to optimize the image quality. In this paper, we present a theoretical framework to address such challenge under the assumption of either variable flip angles or a constant flip angle. In addition, we analyze the gradient arrangement to perform fast imaging to overcome intrinsic short decoherence in solids. Hyperpolarized diamonds imaging is demonstrated as a prototypical platform to test the theory.

**Keywords:** hyperpolarization; magnetic resonance imaging; flip angle

## 1. Introduction

NMR is central to many chemical, biological and material analysis due to the rich chemical information it can provide[1][2][1,2]. MRI, as the imaging counter part of NMR, is a powerful tool in medicine and biology[3][3,4]. However, the sensitivity of both techniques relies on nuclear spin polarization, which is intrinsically low at thermal equilibrium. One compelling approach to tackle this insensitivity is hyperpolarization. This approach brings the nuclear spin polarization level beyond thermal equilibrium to produce many orders of magnitude higher signal. Routes to hyperpolarization includes dynamic nuclear polarization (DNP)[5], parahydrogen induced hyperpolarization (PHIP)[6], as well as chemically-induced DNP (CIDNP)[7]. While the methods of hyperpolarization can be applied in both liquids and solids, hyperpolarized solids are particularly attractive as an imaging agent in nano-medicine[8], or as a polarization hub to deliver hyperpolarization for general chemicals[9]. However, challenges remain on how to image hyperpolarized solids given the none-replenishable nature of the polarization and short coherence times of solids.

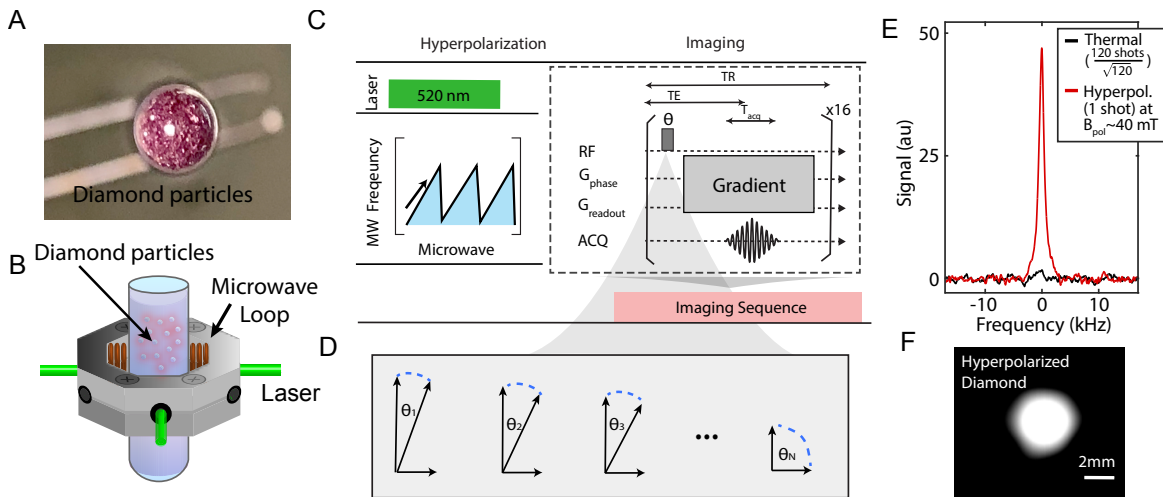
In the work, we use diamond particles (Figure 1A) as a prototypical platform to test the imaging sequences (Figure 1C, D) and to provide some theoretical understanding of the results as well as some insight into sequence design for imaging similar hyperpolarized materials. The hyperpolarization in diamond is enabled by one type of special atom-like defect – the Nitrogen Vacancy (NV) center[10] and a recently developed protocol[9][11][9,11]. The electronic spins of **nitrogen-vacancy (NV) centers can be NV centers are** optically polarizable to  $\approx 99\%$  at room temperature[12], and their long coherence time ensures its efficiency at polarizing surrounding  $^{13}\text{C}$  nuclear spins via chirped MW (Figure 1B, C).  $^{13}\text{C}$  imaging of natural abundance diamond powders (Figure 1F) is only possible with

33 such ~~hyperpolarized highly polarized~~ signal (Figure 1E). ~~<sup>13</sup>C imaging of hyperpolarized diamonds~~  
34 ~~The ability to image micron/nanodiamonds through MRI~~ can open up possibilities in directions  
35 including physics, chemical and biological analysis. For instance, hyperpolarized diamond particles  
36 ~~that "light up" in MRI mode~~ can potentially be applied as a targeting and tracking agent given their  
37 bio-compatibility and surface modifiability [11,13–15]. Additional advantage of high surface-to-volume  
38 ratio can also enable polarization transfer to external nuclei when brought into close contact with other  
39 chemicals for high-SNR and high-resolution NMR [16]. ~~The ability to image the diamond particles~~  
40 ~~can pave a way to such biomedical and chemical analysis applications.~~

41 The analysis of the imaging sequence for a diamond prototypical system relies on a theoretical  
42 framework we develop herein for imaging hyperpolarized solids in general. The theoretical framework  
43 considers two major components of an MRI sequence – flip angle and gradients (Figure 1C), which  
44 determine the quality of an MR image.

45 In an MRI sequence, a radio frequency pulse is normally applied at the beginning of each  
46 repetition, in order to rotate the magnetization from z direction to the xy plane, so that the nuclear  
47 Larmor precession can be detected. The angle of such rotation is referred as flip angle. In conventional  
48 MRI without hyperpolarization, the z magnetization can be recovered after each repetition by ~~the~~  $T_1$   
49 relaxation ~~process~~. In contrast, for the ~~case cases~~ of hyperpolarization, the ~~gain of the signal stems~~  
50 ~~from hyperpolarization process; however~~ ~~initial polarization is much higher beyond the equilibrium~~  
51 ~~state; thus~~, relaxation tends to reduce it towards a ~~thermal equilibrium level. On the other hand, the~~  
52 ~~much lower level. As a results, some sequence design principles in conventional MRI no long hold in~~  
53 ~~such cases, and it requires careful engineering of flip angles to be suited for imaging hyperpolarized~~  
54 ~~objects. The~~ high level of the magnetization, if effectively distributed, can enhance the image SNR and  
55 resolution by orders of magnitude.

56 Not only does flip angle have to be designed uniquely for hyperpolarized solid state imaging,  
57 better arrangement of the gradient and pulses are critical as well. As a result of the nature of solids,  
58 static coupling between nuclei leads to short coherence times. This ~~indicates suggests~~ that one has to  
59 either perform imaging rapidly or apply pulse sequences to ~~prolong  $T_2$  protect coherence~~. We present  
60 strategies ~~with both fast imaging and decoupling that either facilitate fast imaging or refocus signals~~  
61 ~~by decoupling sequences~~ with a focus of  $^{13}\text{C}$  MRI in diamonds.



**Figure 1. Experiment schematic.** (A) A picture of diamond particles ( $\approx 200\mu\text{m}$  in size) contained in an NMR tube as an imaging phantom (taken from the bottom of a NMR tube). (B) Green laser excitation and MW irradiation is applied on the sample in order to transferred polarization to lattice  $^{13}\text{C}$  nuclei from optically polarized NV- electrons in the microscopic scale. (C) Experimental protocol of hyperpolarizing and imaging diamonds.  $^{13}\text{C}$  hyperpolarization occurs at 38mT under MW sweeps across the NV-ESR spectrum, and then transferred to a MRI machine for imaging. Flip angles and gradient arrangement determine the quality of the MRI. (D) Illustration of flip angles for the  $n$ th repetitions. (E) Typical signal enhancement by hyperpolarization, showing signal gain against signal at 7T. For a fair comparison, the noise in both is normalized to be 1 (dash line). (F) A typical MR image of diamond phantom ~~of in~~ (BA).

## 62 2. Results

### 63 2.1. Image equation

64 We analyze the dynamic of the magnetization change under certain flip angle pulses and ~~present~~  
 65 ~~theoretical~~ theoretically present optimal solutions. In this section, we consider two major scenarios,  
 66 i.e. dynamically changeable flip angles and a constant flip angle over different repetitions. We also  
 67 consider two metrics for our optimization – total magnetization, which corresponds to total signal of  
 68 the image, as well as and the uniformity of the signal across repetitions.

More explicitly, we write down the signal equation of an MR image in terms of the xy plane magnetization  $M_x$  [17]:

$$S(k_x, k_y) = \iint M_x(x, y, k_x, k_y) e^{-i2\pi(k_x x + k_y y)} e^{-t(k_x, k_y)/T_2^*} dx dy \quad (1)$$

where  $k_x = \gamma/2\pi \int_0^t G_x(t) dt$ ,  $k_y = \gamma/2\pi \int_0^t G_y(t) dt$  ( $\gamma$  is the gyromagnetic ratio, and  $G_x$ ,  $G_y$  are gradients along x and y axis). Note that this signal equation takes into consideration that the transverse magnetization  $M_x$  as a function of  $k_x$  and  $k_y$  can be different for each repetition ~~which is associated with certain  $k_x$  or  $k_y$ . We can write~~. This dependence can be expressed as:

$$M_x(x, y, k_x, k_y) = K(k_x, k_y) \cdot \rho(x, y) \quad (2)$$

where  $K(k_x, k_y)$  ~~which~~ (we refer as *magnetization factor*) is the factor ~~induced by representing~~ non-uniform excitation in each repetitions (for instance a progression of small tip angle pulses), and  $\rho(x, y)$  is the nuclear spin density at location  $(x, y)$ . ~~Fourier transform this to the real space, we get the image~~ Performing Fourier transform of  $S(k_x, k_y)$ , we obtain the image represented in the real space:

$$I(x, y) = \mathcal{F}(K) * \mathcal{F}(e^{-t(k_x, k_y)/T_2^*}) * \rho(x, y) \quad (3)$$

69 ~~Where~~, where  $\mathcal{F}$  represents Fourier transformation and  $*$  represents convolution. ~~Taking Note that if~~ <sup>by</sup>  
 70 ~~taking~~ the limit of  $t \ll T_2^*$ , and assuming uniform excitation cross different repetition, the Equation  
 71 (3) reduces to  $\mathcal{I}(x, y) = \rho(x, y)$ .

72 The image equation (Equation (3)) is different from a typical image equation as the first term  
 73 represents the effect of flip angles, which is special to the case of hyperpolarization. In repetition  $n$ ,  
 74 we denote this effect to be  $K_n$ . In the case of Cartesian sampling, we can write  $n = k_x$  without losing  
 75 generality.

## 76 2.2. Flip angle consideration

77 How does  $K_n$  depend on the flip angle  $\theta$ ? We address this question by considering ~~a two cases:~~ <sup>whether</sup>  
 78 dynamically changing flip ~~angle angles~~ and a constant flip angle. ~~In practice, wether one has the~~  
 79 ~~ability to program the flip angle for each repetition on the MRI machine determines which case will~~  
 80 ~~be utilized.~~

**Variable flip angle** – First we consider the most general scenario where one has control on the  
 flip angle of each repetition. This stems from an intuitive demand that magnetization remains same in  
 each repetition, similar to the magnetization in saturation recovery sequences. More specifically, if  
 we implement an imaging sequence with ~~repetition TR a repetition time TR~~ to a nuclear spin system  
 with relaxation time  $T_1$  ~~and an~~ equilibrium magnetization  $M_0$ , we can write the dynamic equation as  
 following [18]:

$$\begin{cases} M_n = (M_{n-1} \cos \theta_{n-1} - M_0) e^{-\frac{TR}{T_1}} + M_0 \\ M_{x,n} = M_n \sin \theta_n \end{cases} \quad (4)$$

81 where we denote ~~in the~~  $n$ th repetition, the flip angle to be  $\theta_n$ , the longitudinal and transverse  
 82 magnetization to be  $M_n$  and  $M_{x,n}$  respectively. Given that magnetization can be written as  
 83 ~~multiplication of the magnetization factor and the spin density:~~  $M_n = K_n * \rho(x, y)$ ,  $M_{x,n} = K_{x,n} *$   
 84  $\rho(x, y)$ , and  $M_0 = K_0 * \rho(x, y)$ , we can eliminate the location information ~~in~~  $\rho(x, y)$ , and simplify the  
 85 dynamic equation in terms of magnetization factor  $K$ .

$$\begin{cases} K_n = (K_{n-1} \cos \theta_{n-1} - K_0) e^{-\frac{TR}{T_1}} + K_0 \\ K_{x,n} = K_n \sin \theta_n \end{cases} \quad (5)$$

The initial magnetization factor in the hyperpolarization case is  $K_{hp}$ , in contrast to the thermal  
 polarization case  $K_0$ . With such initial condition, we solve the ~~dynamic equation recurrent dynamic~~  
~~equation (Equation (5))~~ and obtain:

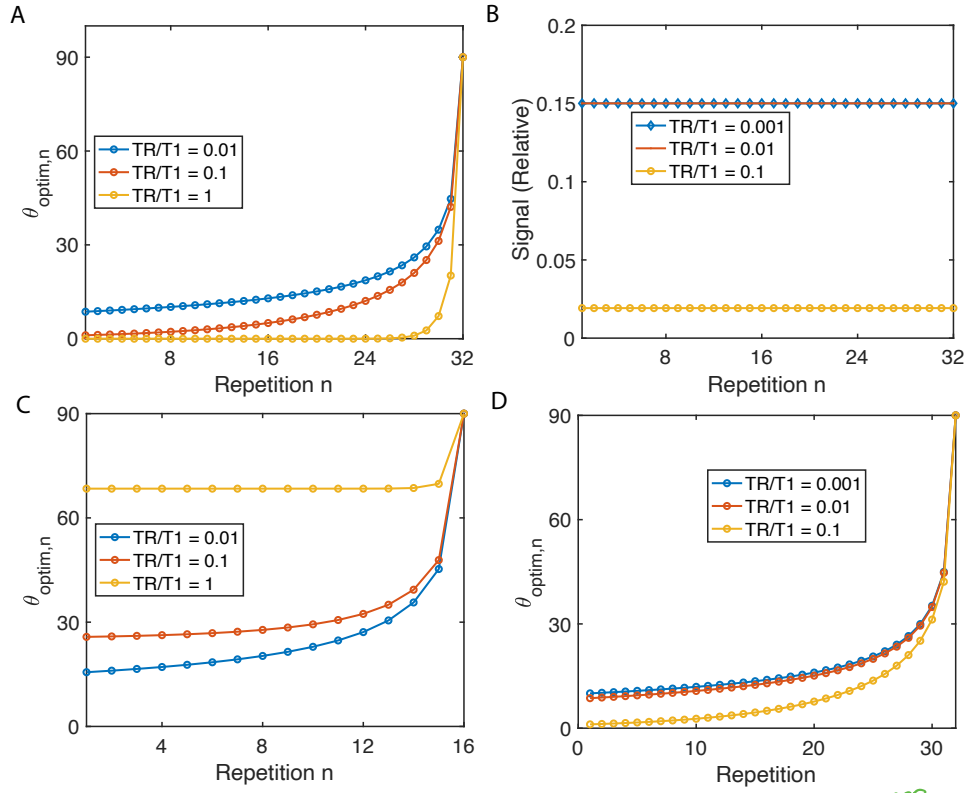
$$K_{x,n} = K_{hp} \left[ \prod_{k=1}^{n-1} (\Gamma \cos \theta_k) + \frac{1}{K_{hp}/K_0} (1 - \Gamma) \times \left\{ \sum_{i=2}^n \prod_{k=i}^{n-1} (\Gamma \cos \theta_k) \right\} \right] \sin \theta_n \quad (6)$$

86 where  $\Gamma = e^{-\frac{TR}{T_1}}$ . We assume hyperpolarization enhances signal much higher than thermal  
 87 signal, suggesting  $K_{hp} \gg K_0$ . With such approximation, we have ~~the~~ leading order  $K_{x,n} =$   
 88  $K_{hp} \left[ \prod_{k=1}^{n-1} (\Gamma \cos \theta_k) \right] \sin \theta_n$ .

89 One of the advantages of having ability to dynamically varying the flip angle is that the transverse  
 90 magnetization  $M_x$  in each repetition can be constant by carefully design the flip angles. This allows  
 91 one to avoid image distortion along the phase encoding direction (further detailed in the Discussion  
 92 section). Applying the condition of  $K_{x,n} = \text{constant}$ , we can obtain (see Appendix A.1):

$$\tan^2 \theta_n = (1 - \Gamma^3) \cdot \frac{\Gamma^{2N-2n-1}}{1 - \Gamma^{2N-2n-1}} \quad (7)$$

93 where  $N$  is the total number of repetitions.



**Figure 2. Variable flip angles for constant signal and maximum signal.** (A) The flip angles to enable constant magnetization in **each acquisition in** a 32 repetition imaging sequence **is** determined based on Equation (7). (B) Implementing flip angles in (A), the relative transverse magnetization signal is simulated taking  $K_{hp} = 1$  and  $K_0 = 10^{-3}$ . (C), (D) The flip angles to maximize the cumulative signal under different TR/T1. *are*

94 As shown in Figure 2A, flip angles have to increase with the number of repetitions in order to  
 95 maintain same transverse magnetization, and all three curves with different TR/T1 converge to  $90^\circ$  to  
 96 saturate all the magnetization. As a result, the relative transverse magnetization stays flat throughout  
 97 the scan confirmed by simulation (see Figure 2B). Such uniform magnetization factor allows  $K(k_x, k_y)$   
 98 to be constant, resulting in  $\mathcal{F}(K)$  to be a delta function, and the reconstructed image  $\mathcal{I}(x, y)$  in Equation  
 99 (3) to be:  $\mathcal{I}(x, y) \propto \mathcal{F}(e^{-t(k_x, k_y)/T_2^*}) * \rho(x, y)$ , immune from image blur caused by excitation.

In addition to constant magnetization, one desires to gain as large cumulative signal as possible, which leads to a different optimization problem.

$$\arg \max_{\theta_n} \{S_{\text{cumulative}} = \sum_{n=1}^N M_{x,n}\} \quad (8)$$

100 If  $\theta_N$  is optimal, it should satisfy:  $\frac{\partial S_{\text{cumulative}}}{\partial \theta_N} = \Gamma^{N-1} \cos \theta_1 \cdots \cos \theta_{N-1} \cos \theta_N = 0$ .  
 Similarly, we can get:

$$\begin{aligned} \frac{\partial S_{\text{cumulative}}}{\partial \theta_{N-1}} &= \Gamma^{N-1} \cos \theta_1 \cdots (-\sin \theta_{N-1}) \sin \theta_N + \Gamma^{N-2} \cos \theta_1 \cdots \cos \theta_{N-1} = 0 \\ \Rightarrow \Gamma \sin \theta_{N-1} \sin \theta_N &= \cos \theta_{N-1} \end{aligned} \quad (9)$$

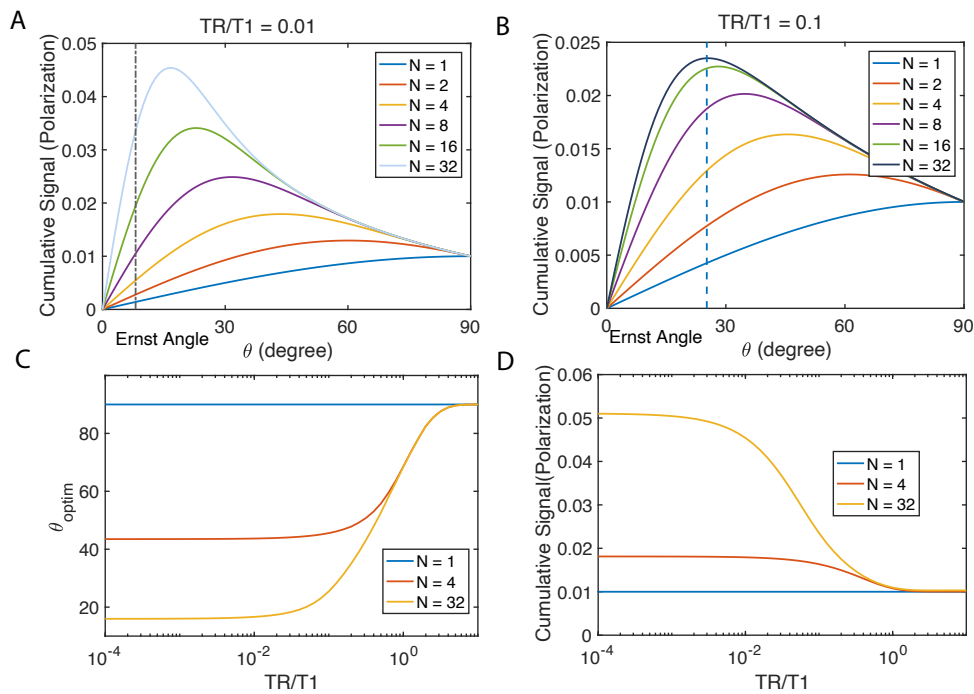
In general, the relationship between two consecutive flip angles is:  $\sin \theta_{n+1} = \Gamma \tan \theta_n$   
 $\sin \theta_{n+1} = \Gamma \tan \theta_n$ . Iteratively solving this sequence from the end where  $\sin \theta_N = 1$  (see Appendix A.2), we have:

$$\theta_n = \tan^{-1} \sqrt{\frac{1}{\Gamma^2} \cdot \frac{1 - \Gamma^2}{1 - \Gamma^{2(N-n)}}} \quad (10)$$

101 And such results of  $N = 16$  and  $32$  are presented in Figure 2C and D.

102 So far, we have derived the design of variable small principle of variable flip angle pulses to  
 103 achieve either constant magnetization or maximum total magnetization. We here briefly comment on  
 104 images we may acquire in these two cases. In the case where there is a fixed transverse magnetization  
 105 in each repetition to start with, the image may display less SNR than the total signal optimized  
 106 case. However, the constant signal guarantees high fidelity due to eliminated distortion in the phase  
 107 encoding dimension. In contrast, in the case of maximum total magnetization, image distortion cannot  
 108 be avoided but the image SNR is optimal.

109 **Constant flip angle** – In spite of the stable magnetization and high cumulative signal that is  
 110 brought by variable flip angles, it posts technical challenges on MRI facilities to implement different  
 111 flip angles in each repetition. A more widely used case is the constant flip angle, where the excitation  
 112 pulse remains pulses remain the same for all of the repetitions. We consider such case in the this  
 113 section and optimize the cumulative signal under such scenario.



**Figure 3. Constant flip angle.** In the simulation,  $K_{\text{hp}} = 10^{-3}$  and  $K_0 = 10^{-5}$ , which is on the same order of magnitude of magnetization with our diamond imaging case at 9.4T. (A) Cumulative signal with different total repetitions  $N$  is displayed when the ratio of  $TR/T1$  is fixed. The black dash line is the Ernst angle, optimal for initial magnetization to be  $M_0$ . (B) Fixing the ratio  $TR/T1$ , we simulate the cumulative signal with different  $N$ . (C) Optimal flip angles and (D) resultant cumulative signals when such angle is restricted to a constant are shown as a function of  $TR/T1$ .

The dynamic equation is similar despite the fact that  $\theta$  is constant:

recurrent

$$\begin{cases} K_n = (K_{n-1} \cos \theta - K_0) e^{-\frac{TR}{T1}} + K_0 \\ K_{x,n} = K_n \sin \theta \end{cases} \quad (11)$$

Solving the dynamic equation:

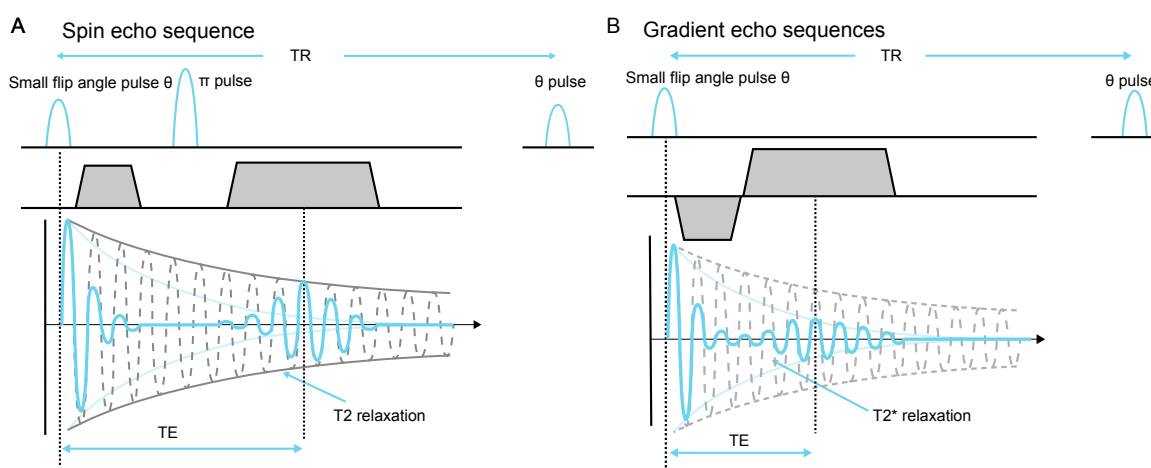
$$K_{x,n} = \pm K_{\text{hp}} (\Gamma \cos \theta)^{n-1} \sin \theta + K_0 (1 - \Gamma) \sum_{k=1}^{n-1} (\Gamma \cos \theta)^{k-1} \sin \theta \quad (12)$$

114 Simulating this process, we observe the change of the magnetization with respect to  $n$  given a  
 115 certain  $\theta$  and TR/T1 in Figure A1. Note that in this case, we do not ignore the first term in Equation  
 116 (12) because constant flip angle can lead to comparable magnitude of the first term with the second  
 117 term.

118 Similarly, we calculate cumulative signal:  $S_{\text{cumulative}} = \sum_{n=1}^N M_{x,n}$  in Figure 3. Not surprisingly,  
 119 there is an optimal flip angle given certain TR/T1 and total number of scans  $N$ . Under such optimal  
 120 angle, the case of  $N = 32$  displays a more than 4 times higher cumulative signal than  $90^\circ$  pulse  
 121 could (Figure 3A). When TR/T1 is less, increasing scan counts may become very effective for signal  
 122 enhancement (Figure 3B). We compare this optimal flip angle with Ernst angle which is the flip angle  
 123 for excitation of a particular spin that gives the maximal signal intensity in the least amount of time in  
 124 the thermal polarization cases. We find that the optimal flip angle deviates from Ernst angle, however,  
 125 approaching it when  $N$  increases.

126 It is difficult to optimize  $S_{\text{cumulative}}$  analytically, and we use a gradient descent method to  
 127 numerically solve the problem, and the result is shown in Figure 3C, D.

### 128 2.3. Gradient consideration



**Figure 4. Spin echo and gradient echo sequence with small flip angle.** (A) The  $\pi$  pulse refocuses dephasing caused by field inhomogeneity, chemical shift, and gradients. (B) The reversed gradient refocuses the effect of gradients. The phase encoding dimension implements same gradient arrangement for both of the two echo sequences, and is omitted here.

129 Gradient arrangement is another critical component in hyperpolarized solid state imaging. This  
 130 determines timing for signal acquisition and k-space sampling trajectory and ultimately dictates image  
 131 SNR, fidelity as well as resolution. Here we consider three categories of gradient arrangement, i.e. spin  
 132 echo, gradient echo, and more exotic sequences. By analyzing different types of sequences, we provide  
 133 insight into the gradient arrangement and sequence parameter determination for a given sample.

134 A typical spin echo sequence with small flip angle is shown in Figure 4. For a certain voxel  
 135  $(x, y, z)$ , we consider the signal at the peak of the echo  $S(TE)$ , which is a good indication of the image  
 136 SNR. This signal within one voxel is subject to decoherence posterior to the flip angle pulse, and the  
 137 decay factor is  $e^{-TE_{se}/T_2}$  (see Figure 4A), where  $TE_{se}$  is the echo time of a spin echo sequence. Similarly,  
 138 in a gradient echo sequence, this factor becomes  $e^{-TE_{ge}/T_2^*}$  (see Figure 4B). When assuming that both  
 139 sequences use the same flip angle strategy, the decay factors imply that if  $TE_{se}/T_2 < TE_{ge}/T_2^*$ , the  
 140 spin echo sequence is favorable for higher signal; otherwise, one should choose gradient echo given  
 141 that the signal at the peak of the echo is higher in such cases.

The RARE (Rapid Acquisition with Refocused Echoes) sequence, also known as TSE (turbo spin echo) is a sequence which takes advantage of multiple spin echo train followed by a single  $\pi/2$  pulse. This sequence is originally designed for saturation recovery, can however be implemented with small



flip angle excitation pulses, which may be enhance SNR in hyperpolarized solid state imaging. In this case, there can be T echo trains following a small flip angle excitation in each repetition. The cumulative signal depends on

$$\sum_{j=1}^N \sum_{k=1}^T e^{-k \cdot TE_{se} / T_2} \quad (13)$$

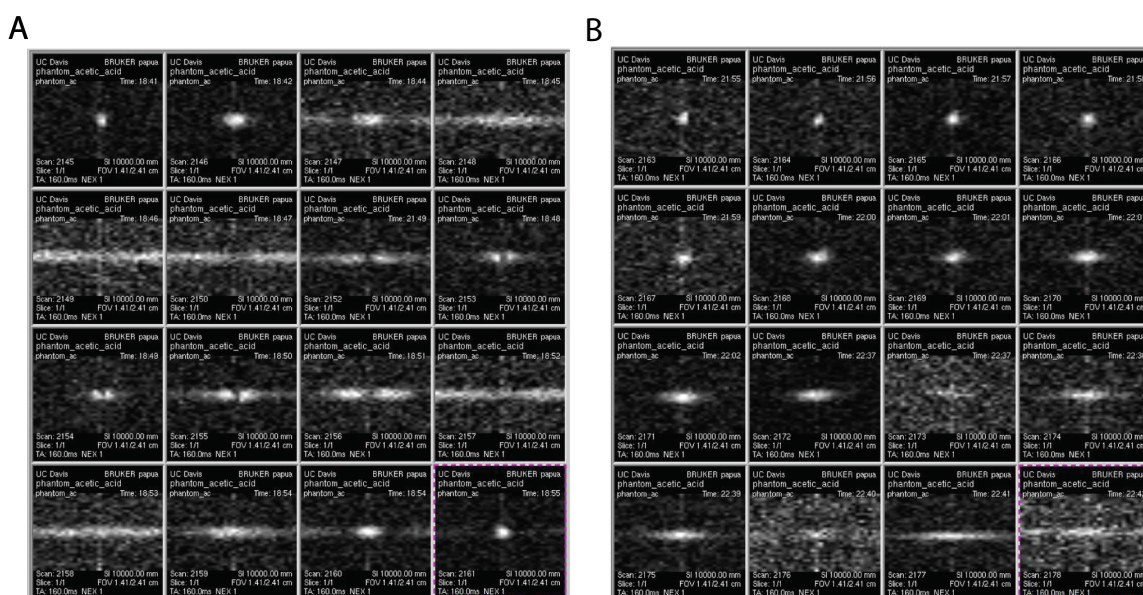
142 where two summations of  $j$  and  $k$  represent repetitions and echo trains respectively. Carefully selection  
 143 of  $N$  and  $T$  can possibly enhance the cumulative signal further than conventional spin echo or gradient  
 144 echo sequences.

145 The sequences that decouple nuclear spins in solids, which we refer to here as “exotic sequences”,  
 146 include magic echo sequence[19], as well as quadratic echo sequence[20]. However, those sequences  
 147 are challenging to calibrate and implement due to the precise requirement of the spacing between  
 148 pulses and the phase of the pulses.

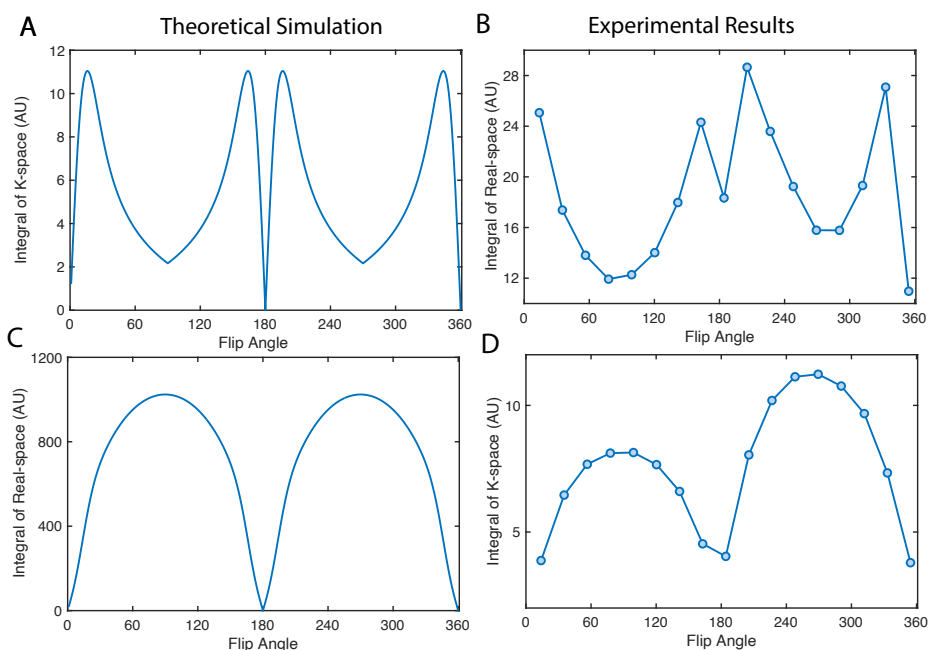
149 Apart from forming spin echo or gradient echo, one can design the gradient arrangement so  
 150 that signal acquisition can start immediately after the excitation pulse. For instance, steady gradient  
 151 on both phase encoding and frequency encoding dimensions can be applied while the acquisition  
 152 channel opens right after RF excitation, which corresponds to a radial trajectory in k-space. Such  
 153 sequences are normally called Ultrashort TE, or UTE sequences[21]. Such methods can eliminate  
 154 the decoherence happening before echo formation, although may have disadvantages in motion and  
 155 gradient imperfection robustness[22].

#### 156 2.4. Hyperpolarized diamond imaging results

157 We test the above simulations using our hyperpolarized diamond imaging system[11]. A 5mm  
 158 NMR tube is filled with diamond particles (average particle size  $\sim 200\mu\text{m}$ ) and the particles are  
 159 tightly held at the bottom of the tube. The MRI images of such phantoms are shown in Figure 5  
 160 with different flip angles. We acquired images with flip angles ranging from  $13 - 333^\circ$  by varying  
 161 pulse length from  $5\mu\text{s}$  to  $80\mu\text{s}$  in Figure 5A, and we zoom in in the range of  $4\mu\text{s}$  to  $19\mu\text{s}$  to identify  
 162 the optimal flip angle in Figure 5B. It turns out that the  $6\mu\text{s}$  presents the highest image fidelity and  
 163 contrast. This shows agreement with Figure 3C, in which diamond particle imaging residents at low  
 164 TR/T1 limit. Our diamond particles have a measured  $T_1$  of 15s and a repetition time TR of 6ms for  
 165 imaging, leading to  $\text{TR}/T_1 \sim 10^{-3}$ , and corresponding  $\theta_{\text{optim}}$  of  $16^\circ$ . Such flip angle can be translated  
 166 as a predicted  $5.5\mu\text{s}$  pulse length. Note that according to our nutation calibration, the pulse duration  
 167  $t_{\text{tip}} = \frac{\theta}{360^\circ} \times 84.58\mu\text{s} + 1.73\mu\text{s}$ , indicating a  $1.73\mu\text{s}$  delay of the pulse application by the MRI machine.



**Figure 5. Diamond MRI with different flip angles.** (A) The pulse durations are 5, 10, 15, ..., 80  $\mu\text{s}$  respectively for each image. We can determine that optimal pulse duration should be within 20 $\mu\text{s}$ . (B) The pulse durations are 4, 5, 6, ..., 19 $\mu\text{s}$  respectively for each image. The text on each image are the frame number, time when the images are taken, and FOV (1.41  $\times$  2.41 cm).



**Figure 6. Total signal in k- and real-space as a function of flip angle.** (A), (B) The integration of absolute value in k-space is simulated and measured using the diamond particle phantom. (C), (D) Display the integration of absolute value in real-space. The simulations are conducted assuming a uniform profile in real-space, i.e.  $\rho(x, y) = \text{constant}$ , in which case only the effect of magnetization factor  $K$  is emphasized. The text on each image are the frame number, time when the images are taken, and FOV: 1.41  $\times$  2.41 cm

168 We can study the total signal in k-space and real-space by taking the integral of intensities across  
 169 all the pixels, shown in Figure 6. The k-space signal maximizes at the optimal flip angle in Figure 6A, B.  
 170 Note that, a 90° pulse can maximize the intensity of the center of the k-space, which is equivalent to  
 171 the integral of real-space intensities (see Figure 6C, D). However such image has no high frequency

172 information, which will be a constant in real-space along x direction. Such effect is precisely illustrated  
 173 in Figure 5 A first image in the second row.

### 174 3. Discussion

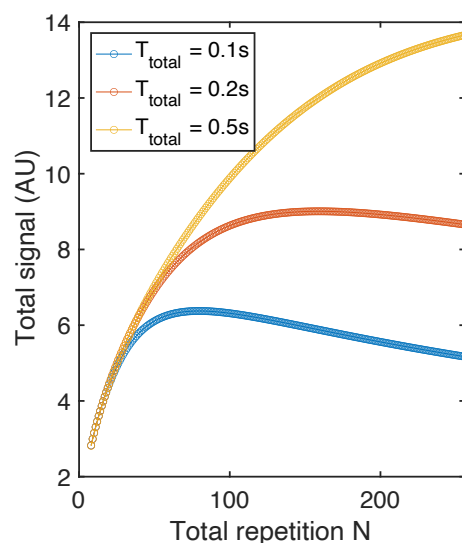
175 In the image equation (Equation 3), the spin density function  $\rho(x, y)$  convolutes with  $\mathcal{F}(e^{-t(k_y)/T_2^*})$   
 176 and  $\mathcal{F}(K_x(k_x))$ . The two terms correspond to two types of blur of the image. The term  $\mathcal{F}(e^{-t(k_y)/T_2^*})$   
 177 caused by  $T_2$  is similar to the linewidth in NMR spectroscopy. The Lorentzian profile leads to a  
 178 resolution limit of  $\propto \frac{1}{\gamma G T_2}$  in real-space, where  $G$  is imaging gradient. The second term is a Fourier  
 179 transform of the profile of magnetization as a function of repetition (see Appendix Figure A1),  
 180 originating from the uniformity of the magnetization distribution over repetitions. The term will  
 181 reduce to 1 when flip angles in Figure 2A is applied. In our experiment, the two types of blur happen  
 182 on x and y direction respectively.

183 Our phase encoding is on x direction, therefore, the stripe line in Figure 5 originates from  
 184 the Fourier transform of the magnetization factor profile  $K$  along  $k_x$  direction. We write down  
 185  $K_x(k_x) = \pm K_{\text{hp}} (\Gamma \cos \theta)^{k_x-1} \sin \theta + K_0 (1 - \Gamma) \sum_{j=1}^{k_x-1} (\Gamma \cos \theta)^{j-1} \sin \theta$ . If we take the 5th frame in  
 186 Figure 5A as an example, the flip angle of that is close to  $90^\circ$ . The magnetization of such pulse  
 187 sequence distributes mainly on the first repetition (green line in Appendix Figure A1A). A nearly  
 188 constant  $\mathcal{F}(K_x(k_x))$  indicates the extreme case of blur – constant intensity along x direction when  
 189 convoluting with  $\rho(x, y)$ .

We would also like to discuss the total signal gained by the small tip angle RARE sequence. From  
 Equation 13, we can tell that increasing number of echo trains will increase the signal, however extends  
 the total acquisition times at the same time. Here we try to determine the optimal sequence design to  
 maximize the total signal given a finite total time  $T_{\text{total}}$ . We take the case where one is allowed to vary  
 the flip angle, and the signal is constant in each repetition (as described in Equation 7). We assume  
 that in each repetition  $TR = TE_{se} \times T$ , where  $T$  is total number of echos within this repetition. We can  
 rewrite Equation 13 to estimate total signal as a function of total repetition number  $S(N)$ :

$$\begin{aligned}
 S(N) &= \sum_{j=1}^N \sum_{k=1}^{T(N)} e^{-k \cdot TE_{se} / T_2} \\
 &= N \cdot M_x(N) \cdot \chi \frac{1 - \chi^T}{1 - \chi}
 \end{aligned}
 \tag{14}$$

190 where  $\chi = e^{TE_{se}/T_2}$  is a constant when minimized  $TE$  is set by instrumentation limit and  $T_2$  is the  
 191 intrinsic property of certain sample. The above derivation used the sum of a geometric sequence. In  
 192 this equation  $M_x = M_0 \times \sin(\theta_1)$  where  $\theta_1$  defined in Equation 7 is a function of  $TR$ , and  $TR = \frac{T_{\text{total}}}{N}$ .  
 193  $T$  can also be written as a function of  $N$ :  $T(N) = \frac{T_{\text{total}}}{N \cdot TE_{se}}$ . We plot  $S(N)$  in Figure 7. We note that  $N$   
 194 values that can maximize  $S(N)$  for  $T_{\text{total}} = 0.1$  s and 0.2 s are  $\sim 70$  and  $\sim 120$  respectively. And when  
 195  $T_{\text{total}}$  is long enough (0.5 s),  $S(N)$  is not yet saturated at  $N = 256$ .



**Figure 7. Total signal with RARE sequence.** The simulation is ~~done~~ conducted based on parameters close to diamonds. ~~Here~~ ( $T_1 = 50s$ ,  $T_2 = 1ms$ ,  $TE = 0.5$  ms). The total signal curve  $S(N)$  maximize at different  $N$  when  $t_{total}$  is set to different values.

## 196 4. Materials and Methods

### 197 4.1. Simulation and optimization

198 The simulations and optimizations are conducted in Matlab, where the “fminunc” function  
 199 is used to numerically optimize the flip angles in Figure 3C, D. In the simulation of Figure 6, the  
 200  $K(k_x)e^{-t(k_x, k_y)/T_2^*}$  component is simulated with  $K(k_x)$  in Equation (12), substituting  $n$  with  $k_x$ .

### 201 4.2. Hyperpolarization and imaging

202 The diamond powder utilized in experiments in Figure 1 has  $\sim 40$  mg mass with natural  
 203 abundance  $^{13}C$ . The particles are purchased from Element6. They are enriched with  $\sim 1$  ppm NV  
 204 centers and fabricated by a high pressure high temperature (HPHT) protocol. The particle size is  
 205 measured in SEM (scanning electron microscopy) images. The face to face distances are  $200 \mu m$  to  $250$   
 206  $\mu m$  and diagonal edge to edge distances are approximately  $400 \mu m$ .

207 The entire experimental setup consists of three parts: a pneumatic field-cycling device, a wide-bore  
 208 9.4T superconducting magnet, an a miniaturized hyperpolarizer[23][24]. The pneumatic field-cycling  
 209 device[11] is uses air flow to rapidly transfer a 5mm NMR tube from low field (40 mT) to the 9.4 T  
 210 detection field, within which a 10 mm  $^1H/^{13}C$  volume coil is installed. The air driven by a pump  
 211 flows in a quartz channel and moves the NMR tube in the channel. Diamond samples are contained  
 212 in the NMR tube. A concave-shaped stopper is located at the bottom end of the channel and a  
 213 rubber stopper is placed at the high field. The transport time of the sample to high field is under 1s,  
 214 much shorter compared to the  $^{13}C$   $T_1$  times (normally on the order of minutes). MR imaging was  
 215 conducted with a Bruker DRX system equipped with microgradients running ParaVision 4 software  
 216 with a modified FLASH pulse sequence. The miniaturized hyperpolarizer is a self-contained unit,  
 217 which encapsulates devices for laser excitation, MW irradiation as well as an electromagnet for field  
 218 fine-tuning. A 1W 520nm diode laser (Lasertack PD-01289) is employed and the beam passes through  
 219 an aspheric lens and a set of anamorphic prisms to form a 4 mm diameter beam. The beam was guided  
 220 by two mirrors and illuminates the sample from the bottom. MW irradiation that drives polarization  
 221 transfer is generated by three voltage controlled oscillator (VCO) sources (Minicircuits ZX95-3800A+).  
 222 For frequency sweeps, the VCOs are driven by phase shifted triangle waves from a home-built PIC  
 223 microprocessor (PIC30F2020) driven quad ramp generator.

224 Please find more details of experimental methods in Ref.[11]

## 225 5. Conclusions

226 In this paper, we studied two major components – small flip angles and gradient arrangement  
 227 in a MRI sequence in the quest for optimal sequences for hyperpolarized solids. Both variable and  
 228 constant flip angles are analyzed, and strategies to achieve maximum cumulative signal or flat signal  
 229 profile are provided. Beyond designing flip angle progressions to take advantage of the significant  
 230 initial magnetization produced by hyperpolarization, we propose to combine these excitation pulse  
 231 progressions with traditional gradient arrangements in spin echo and gradient echo sequences in order  
 232 to accommodate short decoherence times in solids. Experimental results of hyperpolarized diamond  
 233 MRI show agreement with theoretical analysis. Beyond diamond particles, this study can provide  
 234 guidance in hyperpolarized solids MRI in systems such as such as silicon[25] and silicon carbide[26]  
 235 particles.

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 240 interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

## 241 Appendix A Derivation

### 242 Appendix A.1 Variable flip angle for constant magnetization

$$K_{x,n} = K_{\text{hp}} \left[ \prod_{k=1}^{n-1} (\Gamma \cos \theta_k) \right] \sin \theta_n = \text{constant} \quad (\text{A1})$$

Since we want to saturate the magnetization at the last pulse, we have  $\sin \theta_N = 1$ . Using such equation, we can first write down the  $K_{x,N} = K_{x,N-1}$  as:

$$K_{\text{hp}} \left[ \prod_{k=1}^{N-1} (\Gamma \cos \theta_k) \right] \sin \theta_N = K_{\text{hp}} \left[ \prod_{k=1}^{N-2} (\Gamma \cos \theta_k) \right] \sin \theta_{N-1} \quad (\text{A2})$$

This implies  $\Gamma \cos \theta_{N-1} \sin \theta_N = \sin \theta_{N-1}$ , and we can get:  $\tan \theta_{N-1} = \sin \theta_N / \Gamma = 1/\Gamma$ . Similarly, if we take the equality between  $K_{x,j}$  and  $K_{x,j-1}$ , the recursion formula is:

$$\tan \theta_{j-1} = \Gamma \sin \theta_j \quad (\text{A3})$$

243 Then, we need to solve  $\theta_n$  based on the equation above. We define  $a_n = \tan^2 \theta_n$ , and we will have:

$$a_n = \frac{a_{n+1}}{1 + a_{n+1}} \cdot \Gamma^2 \quad (\text{A4})$$

This is equivalent to:

$$\frac{1}{a_n} = \left( \frac{1}{a_{n+1}} - \Gamma^2 \right) \Gamma^2 \quad (\text{A5})$$

Solving the series, we can get:

$$a_n = (1 - \Gamma^3) \cdot \frac{\Gamma^{2N-2n-1}}{1 - \Gamma^{2N-2n-1}} \quad (\text{A6})$$

which leads to:

$$\tan^2 \theta_n = (1 - \Gamma^3) \cdot \frac{\Gamma^{2N-2n-1}}{1 - \Gamma^{2N-2n-1}} \quad (\text{A7})$$

244 *Appendix A.2 Variable flip angle for maximum cumulative magnetization*

With

$$\Gamma \tan \theta_{j-1} = \sin \theta_j \quad (\text{A8})$$

We define  $a_n = \tan^2 \theta_n$ , and we will have:

$$a_n = \frac{a_{n+1}}{1 + a_{n+1}} \cdot \frac{1}{\Gamma^2} \quad (\text{A9})$$

This is equivalent to:

$$\frac{1}{a_n} = \left( \frac{1}{a_{n+1}} - \Gamma^2 \right) / \Gamma^2 \quad (\text{A10})$$

Solving the series, we can get:

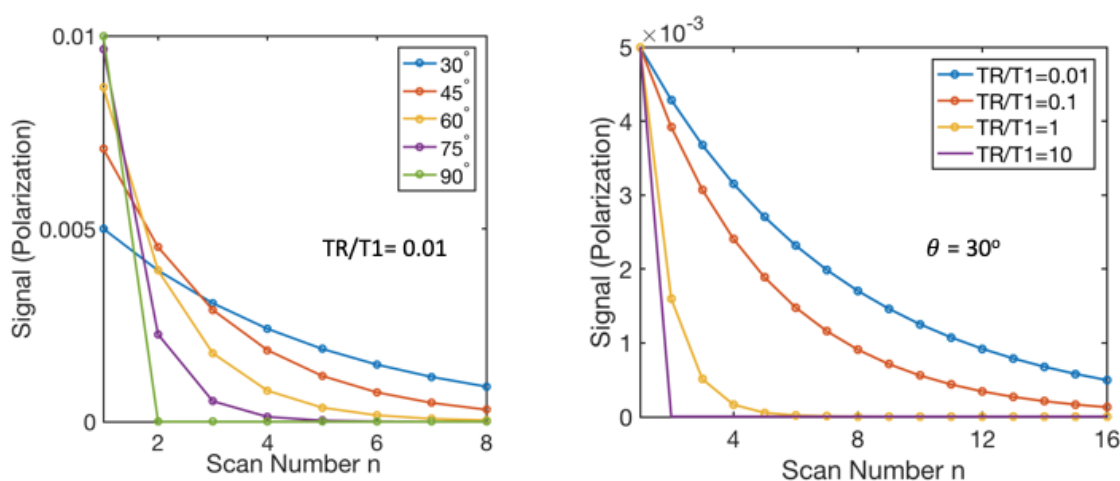
$$a_n = \frac{1}{\Gamma^2} \cdot \frac{1 - \Gamma^2}{1 - \Gamma^{2(N-n)}} \quad (\text{A11})$$

which leads to:

$$\tan^2 \theta_n = \frac{1}{\Gamma^2} \cdot \frac{1 - \Gamma^2}{1 - \Gamma^{2(N-n)}} \quad (\text{A12})$$

245 **Appendix B Magnetization simulation**

246 The magnetization of each repetition when applying constant flip angle is presented.



**Figure A1.** Simulation of signal of each individual repetition as a function of scan number of given TR/T1 in (A) and given  $\theta$  in (B). In the simulation, we assume  $K_{hp} = 10^{-3}$  and  $K_0 = 10^{-5}$ , which approximates the magnetization with our diamond imaging case at 9.4T.

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