Published in final edited form as:

Z Phys Chem (N F). 2017 March ; 231(3): 689–703. doi:10.1515/zpch-2016-0843.

Concept of Phase Cycling in Pulsed Magnetic Resonance Using Sinusoidal Magnetic Field Modulation

Mark Tseytlin^{a,b,c}

^aDepartment of Biochemistry, School of Medicine, West Virginia University, Morgantown, West Virginia, USA

^bCenter for EPR Imaging In Vivo Physiology, Department of Radiation and Cellular Oncology, University of Chicago, IL, USA

^cIn vivo Multifunctional Magnetic Resonance center, Robert C. Byrd Health Sciences Center, West Virginia University, Morgantown, WV, USA

Abstract

In conventional pulsed magnetic resonance suppression of unwanted signals is achieved by changing pulse phases with respect to the reference signal and spin magnetization phase. This method is called phase cycling. An alternative approach is suggested to separate the unwanted signals from the spin echo by using magnetic field modulation. Precession frequency of the spins, and therefore phases of free induction decays and echo signals, can be controlled by the selection of modulation parameters. This enables phase cycling. Since the signal is detected in the presence of the changing magnetic field, which drives spin precession, the echo signal is frequency-modulated. Numerical transformation into an accelerating reference frame associated with the Larmor frequency restores the signal to a form that would have been observed in the absence of modulation. The suggested phase cycling method is analyzed in detail for the two pulse spin echo case.

1. Introduction

1.1 Underlying Concept

Phase cycling is routinely used in magnetic resonance to remove background signals and to suppress unwanted free induction decays (FID) and spin echoes [1, 2]. By alternating phases of the excitation pulses, followed by either addition or subtraction of the measured signals, one can amplify the echo of interest with respect to other components of the signal that overlap with the echo. In some experiments, the unwanted signals, such as resonator ring-down, are difficult to remove completely because the excitation power is many orders of magnitude larger than that produced by the spin system response. The subtracted residual of two strong ring-down signals may be comparable to the amplitude of the echo. An alternative/complimentary approach to phase cycling that is expected to further suppress the unwanted signals is investigated in this paper. This approach is based on the fact that the

magnetization vector, $\mathbf{M}$, changes, not only under the influence of the alternating magnetic field, B_1 , at the resonance conditions, but also precesses about the external magnetic field, B_0 , parallel to the z-axis, with the angular frequency $\omega_0 = \gamma B_0$. The precession frequency, ω_0 , is called the Larmor frequency. In the magnetic resonance experiment, the projection of $\mathbf{M}$ on the xy-plane, $\mathbf{M}_{xy}$, is the observable. It revolves with ω_0 in the laboratory frame of coordinates. By increasing or decreasing the external magnetic field, one can alter the precession frequency with respect to the selected reference, which is often phase-locked to the excitation source. In the rotating frame associated with the reference, changes to the external magnetic field are observed as phase changes in $\mathbf{M}_{xy}$. The additional phase gained during free evolution in the time interval $[a, b]$ due to the time-dependent magnetic field, $B_z(t)$, can be found by integration of the time-dependent component of the Larmor frequency $\omega_L(t)$:

$$\varphi(a, b) = \int_a^b \omega_L(t) dt = \gamma \int_a^b B_z(t) dt, \quad B_1(a \leq t \leq b) = 0 \quad (1)$$

$B_z(t)$ in Eq. (1) can be selected in the experiment to rotate $\mathbf{M}_{xy}$ by a desired angle, $\varphi(a, b)$, with respect to the reference. This rotation produces result analogous to changing the pulse phase in the conventional phase cycling method. For example, consider a two-step cycle used to suppress FID contributions originated from the second 180° pulse in the spin echo experiment:

$$90_{+x}^0 - \tau - 180_{+x}^0 - \tau - echo \quad (2a)$$

$$90_{+x}^0 - \tau - 180_{-x}^0 - \tau - echo \quad (2b)$$

Summation of the echo signals generated by the pulse sequences in Eq. (2a) and Eq. (2b) results in the suppression. Changing the phase of the second pulse ($180_x^0 \rightarrow 180_{-x}^0$) can be substituted by rotation of the magnetization in the xy-plane between the 1st and 2nd pulses using changing magnetic field:

$$90_{+x}^0 - \tau - \pi - 180_{+x}^0 - \tau - echo \quad (3)$$

In Eq. (3), the subscript π of τ indicates that the magnetization vector changed phase by π during free evolution in time τ , $\varphi = \pi$ in Eq. (1). Because the relative phases between the second pulse and the magnetization vector are the same for both Eqs. (2) and (3), either can be used to suppress an FID signal after the second pulse.

The phase cycling method described above can be used for both nuclear magnetic resonance (NMR) and electron paramagnetic resonance (EPR). However, the method is more likely to be implemented in paramagnetic resonance, as field modulation is routinely used in EPR.

For this reason, the following theoretical analysis and numerical examples are given for EPR, and γ in Eq. (1) refers to the gyromagnetic ratio for an electron.

1.2 Field-step Pulsed EPR

The method of varying B_0 in pulsed EPR is not novel. For example, it is used in field-step electron-electron double resonance (FS-ELDOR) to measure weak interactions between spectrally-separated electron spins [2–9]. If two interacting spin systems, A and B, resonate at different frequencies, and if this difference is smaller than the resonator bandwidth (BW), an ELDOR signal is observed by exciting A spins at frequency f_A and B spins at frequency f_B [2]. If $|f_A - f_B| > \text{BW}$ for a loaded resonator, one can artificially lower the resonator quality factor (Q) to increase the BW at the expense of reducing both detection sensitivity and excitation efficiency. Two alternative methods have been implemented to widen the excitation/detection range that do not require lowering the Q . One approach is to design and build a bi-modal resonator with two modes operating at f_A and f_B [10, 11]. The frequency difference $|f_A - f_B|$ can be selected to be as large as needed for the experiment. The major challenge for bi-modal resonator design is achieving sufficient and stable isolation between the modes. The second approach is to use a single-mode resonator and change the external magnetic field. In this case, A spins are first excited by a pulse in B_0 , then the field is jumped to the new value, $B_0 + B_z$, and B spins are excited by a second pulse at the same frequency ($f_A = f_B$). A standard single-mode resonator equipped with field-jump coils can be used if it does not substantially attenuate amplitude or distort the shape of the field-jump due to eddy-currents induced on the conducting surfaces of the resonator [5, 7]. Dubinskii *et al.* [12] designed a system that produced sub-microsecond field jumps up to 160 G. In this design, a number of mutually-contradicted technical difficulties were addressed. To shorten the rise and after-pulse fall times, low-inductance coils were used that resulted in low current-to-field transformation factor, or coil constant. Short pulses induce eddy-currents in the surrounding conducting components of the resonator, causing mechanical vibrations that lead to spatial and temporal distortion of the field ‘observed’ by the spins. An abrupt change of the magnetic field alone may generate electromagnetic waves with components close to the resonator frequency, producing an associated ring-down in the resonator.

1.3 Sinusoidal Field Modulation in Pulsed EPR

The severity of the technical challenges described above can be substantially reduced if the field-jump is replaced by sinusoidal modulation. This was first realized and implemented in the Schweiger laboratory [13]. The advantages of the modulation method are: (i) resonating coils with a capacitor permits higher inductance and therefore improved efficiency; (ii) lack of transient effects: within a few modulation cycles, the amplitude of the modulation becomes steady; (iii) eddy-currents produce sinusoidal magnetic field that depending on the geometry may degrade spatial homogeneity of the modulation but not its single-tone time dependency.

The schematic of the field-modulated pulse experiment is shown in Fig. 1. Both the excitation pulses and the spin echo occur at the zero-crossing points of the field modulation:

$$B_z(t) = 0.5 B_{pp} \sin(2\pi f_m t), \quad (4)$$

and, since $B_z(t) = 0$, in the resonance field B_0 . In Eq. (4), B_{pp} is the peak-to-peak modulation amplitude and f_m is the modulation frequency. The magnetization phase gain due to $B_z(t)$ can be calculated by substitution of Eq. (4) in Eq. (1):

$$\varphi(a, b) = \alpha (\cos \theta_a - \cos \theta_b), \quad \alpha = \frac{\gamma B_{pp}}{4\pi f_m}, \quad \theta_t = 2\pi f_m t \quad (5)$$

Assuming the pulse lengths are much shorter than the delay, τ , in Fig. 1, the phases gained between the pulses and the second 180° pulse and echo (see Fig. 1) are as follows:

$$\varphi(0, \tau) = -\varphi(\tau, 2\tau) = 2\alpha \quad (6)$$

After the first 90° pulse applied along the x-axis (solid red arrow, Fig. 1b), the magnetization vector is directed along -y (solid blue arrow, Fig. 1b). It then rotates by 2α due to $B_z(t)$ (dashed blue line, Fig. 1b). The second 180° pulse (solid red arrow, Fig. 1c) inverts the magnetization with respect to the x-axis (solid blue arrow, Fig. 1c), and the magnetization rotates by -2α during free evolution in the time interval $[\tau, 2\tau]$ to form an echo (dashed blue arrow, Fig. 1c). As a result, the echo signal, which appears at $\varphi(\alpha) = -4\alpha + \pi/2$, has gained phase with respect to the echo observed with no modulation ($\alpha = 0$):

$$\Delta\varphi = \varphi(\alpha) - \varphi(0) = 4\alpha \quad (7)$$

Eq. (7) describes the phase of M_{xy} at the point of maximum echo amplitude only, as the phase is constantly changing.

For polycrystalline samples with large g-anisotropy, Eq. (7) must be corrected to include the Larmor frequency dependence on the orientation-dependent g-factor:

$$\Delta\varphi = 4\alpha \frac{g}{g_e}, \quad (8)$$

Here, g is the g-value for a selected orientation and g_e is that for the free electron. Eichel and coauthors [13] developed the Zeeman-resolved EPR (EZ EPR) method based on Eq. (8). By changing B_{pp} together with the external magnetic field, B_0 , they were able to separate contributions from different orientations in a 2D experiment. A modified version of EZ EPR in which they implemented a three-pulse stimulated spin echo sequence was later developed by the same group [14]. Dependence on g in Eq. (8) that is useful for EZ EPR also restricts the proposed phase cycling method to paramagnetic centers in solution, where g-anisotropy is effectively averaged, and in solid state if the anisotropy is small. Implementation of the

method to solid transition metal ion complexes may be problematic. A detailed analysis of this limitation is given in the next section.

2. Theory and Numerical Simulations

2.1 Numerical Integration of the Bloch Equations

To verify the theoretical analysis provided below, the Bloch equations with time-dependent external magnetic field and excitation pulses were numerically integrated using a Matlab ode45 solver with the absolute error tolerance of $1e-8$. The modulation amplitude, B_{pp} , in Eq. (4) was varied, and the modulation frequency was $f_m = 1$ MHz. Both pulse lengths were 40 ns, and pulse amplitudes were selected to produce 90° and 180° turning angles. Longitudinal (T_1) and transverse (T_2) relaxation times were 1000 ns and 700 ns, respectively. A series of solutions for $\mathbf{M}_{xy}$ were obtained with constant offsets of the external field in the interval from -5 to 5 G using 80 mG steps. These solutions were summed with different weighting factors to simulate inhomogeneous broadening of Gaussian shape and 1.6 G width measured as the full width at half magnitude.

2.2 Transformation to the Accelerating Reference Frame

Transformation into the rotating frame was first implemented in frequency swept rapid scan NMR [15] and correlation NMR spectroscopy [16] in the 1970s. The external magnetic field was kept constant and, as a result, the Larmor frequency was not changing. Nevertheless, signals oscillating with accelerating frequencies were observed. What appeared to be changes in the Larmor frequency were caused by use of the same RF source to generate both the sweeping excitation and the reference, which was convenient from an engineering standpoint. The transformation helped eliminate the effect of the changing reference. In EPR, the source frequency, as well as the reference, do not change. The transient effects observed in the form of accelerating oscillations are due to the varying Larmor frequency.

In the experiment shown in Fig. 1, the Larmor frequency of the spins is constantly changing due to field modulation, $B_z(t)$. As a result, the observed $\mathbf{M}_{xy}$ component of the magnetization vector oscillates with respect to the ω_0 -associated reference frame:

$$\mathbf{M}_{xy}(t) = M_{xy}(t)(\mathbf{e}_x \cos \varphi_t + \mathbf{e}_y \sin \varphi_t), \quad (9)$$

$$\varphi_t = \varphi(0, t) = \alpha(1 - \cos \theta_t). \quad (10)$$

In Eq. (9), the initial phase is selected to be with respect to the x-direction in the reference frame (vector $\mathbf{e}_x$), and $M_{xy}(t)$ is the amplitude of vector $\mathbf{M}_{xy}(t)$. Time-dependence of the amplitude is due to spin relaxation. Eq. (10) is derived from Eq. (5) by substitution $\theta_t(0) = 0$.

Oscillating signals are routinely observed in continuous wave (CW) rapid-scan EPR (RS EPR) [17]. After rapidly passing through resonance, the magnetization vector freely precesses as described by Eq. (9) and FID-like signals are observed that oscillate with an

accelerating frequency. Similar behavior is expected to be observed for FIDs and echo signals in field modulated pulsed EPR because the magnetic field is changing in the time of measurement. Results of numerical integration of the Bloch equations for the experiment in Fig. 1 are shown in Figs. 2a and 2b. FID and echo oscillations caused by the changing magnetic field may be observed. In some pulse experiments, the echo intensity is measured as a single point at the maximum echo amplitude ($\theta = 360^\circ$ in Fig. 2) and the remainder of the echo is ignored. However, if the signal-to-noise ratio must be improved through echo integration, or if the entire echo must be measured, as in EPR imaging, the observed signal must be transformed into a form convenient for further analysis. As in RS EPR [17], this can be done by changing the experimental reference frame that rotates with constant frequency, $\omega_0 = \gamma B_0$, to one that is associated with the changing Larmor frequency. The time-dependent phase difference between the constant frequency and the accelerating frames is given in Eq. (10). Numerical transformation of the measured signal into the new frame can be achieved by multiplication:

$$s'(t) = s(t) \exp(-j\varphi_t) \quad (11)$$

In Eq. (11), $s'(t)$ and $s(t)$ denote the EPR signal before and after the transformation, respectively. In the accelerating frame, $s'(t)$ does not gain additional phase, φ_t , because the frame itself rotates by φ_t . The results of the transformation for signals in Figs. 2a and 2b are shown in Figs. 2c and 2d. Summation of the signals in Figs. 2c and 2d would eliminate the second FID. Note that a relatively small increase in the modulation amplitude from 9 G to 10 G does not significantly change the shape of the signal but is sufficient to flip the second FID component. It is because of the cumulative effect of integration in Eq. (1). As a result of the transformation via Eq. (11), the phases of the pulses applied in the xy-plane become time-dependent in the accelerating frame. A pulse applied along the x-direction in the constant-frequency frame gains an additional phase, $-\varphi_t$, and may be chosen, for example, to be along the y-direction in the new frame. By selection of the modulation amplitude and/or frequency, one can controllably change the B_1 phase with respect to the magnetization without physically changing it within the hardware. Fig. 3 shows the magnetization vector evolution described in Figs. 1b and 1c after transformation with Eq. (11). Immediately following the first 90° pulse applied along the x-axis (red arrow, Fig. 3a), magnetization (blue solid arrow) is along -y. During the delay, τ , magnetization becomes dephased along the -y direction, and B_1 gains an additional phase. When the second 180° pulse is applied along the x-axis in the constant-frequency frame, it has gained -2α phase in the accelerating frame (red dashed arrow). The 180° pulse flips magnetization with respect to the -2α position, and the echo is refocused at $-4\alpha + \pi/2$ (dashed blue arrow, Fig. 3b). As a result, the first FID retains its $-\pi/2$ phase, the second FID gains an additional -2α phase, and the echo will appear at $-4\alpha + \pi/2$. The phase dependencies for two FIDs and echo can be expressed in the form of a three component vector, respectively:

$$\Phi = \begin{pmatrix} -\pi/2 \\ -2\alpha - \pi/2 \\ -4\alpha + \pi/2 \end{pmatrix} \quad (12)$$

Numerical integration of the Bloch equations with the same parameters as described above was performed to evaluate Φ as a function of α (Fig. 4) for the purpose of comparison with the analytical expression Eq. (12), which was derived under the assumption of negligibly small pulse lengths. Computational phases are shown for Φ_2 (circles) and for Φ_3 (diamonds). Corresponding phases computed using Eq. (12) are shown as solid line for the second FID and dashed line for the echo. $\Phi_1 = -\pi/2$ is not plotted in Fig.(4).

2.3 Phase Cycling

The phase difference with respect to two different α values is as follows:

$$\Delta\Phi = \begin{pmatrix} 0 \\ 2 \\ 4 \end{pmatrix} \Delta\alpha \quad (13)$$

The fact that Φ_3 changes twice as fast compared to Φ_2 in Eq.(13) enables phase cycling. If the modulation parameters are chosen to make $\alpha = \pi/2$, the third element in Eq.(13) becomes equal to 2π and the echo phase remains unchanged. In contrast, $\Phi_2 = \pi$ and the second FID signals is inverted.

The lowest modulation amplitude suitable to cycle out the second FID is achieved for $\alpha = \pm\pi/4$ (see Fig. 4). Summation of two signals corresponding to $\alpha = -\pi/4$ (Fig. 5a) and $\alpha = +\pi/4$ (Fig. 5b) eliminates the second FID (Fig. 5c). If $\alpha = \pm\pi/8$, $\alpha = \pi/4$ and $\Phi = (0, \pi/2, \pi)$. In this scenario, the echo signal is inverted with respect to the first FID. Simultaneously use of the standard B_1 -based phase cycling to suppress the second FID and the field modulation method to eliminate the first FID can be used. The results are shown in Figs. 5d, 5e, and 5f.

2.4 Limitations

As described previously, the use of field modulated phase cycling is problematic for slowly tumbling or immobilized samples having large g-factor anisotropy. To quantitatively estimate the limitation imposed by Eq. (8), a very small phase deviation of one degree is assumed to be acceptable:

$$\delta\varphi = 4\alpha \frac{\delta g}{g_e} \leq \frac{\pi}{180}, \quad \delta g = g_{\max} - g_{\min}, \quad (14)$$

By substituting $\alpha = \pi/4$ into Eq. (14), the upper limit for variation in g is calculated to be $\delta g = 0.011$. To put this value in perspective, most spin probes used in EPR spectroscopy and imaging have $\delta g = 0.006$ [18, 19].

The experiment described in Fig. 1 requires time synchronization between the modulation and pulses, which imposes an additional constraint. Resonance excitation happens at the zero-crossing points of the sinusoid. As a result, τ must be equal to the half-period of the modulation. There are two approaches to solve this problem. The first is to change the modulation frequency, which may require a computer-controlled variable capacitor if resonating the modulation coils is required. An arbitrary waveform generator with remote control capability may be needed for the experimental implementation. It will help to control not only the frequency but also amplitude and phase of the modulation and to synchronize modulation with data acquisition. The second approach stems from the fact that phase ϕ_t in Eq. (10) is periodic. As a result, multiple discrete values of τ are equivalent from the phase cycling standpoint:

$$\tau = (0.5 + k)P, \quad P = 1/f_m, \quad k \in N, \quad (15)$$

In Eq. (15), P is the modulation period. The second approach can be implemented in EPR imaging, where several τ values are used to determine single exponential decay rates [20] in a given voxel. In addition, if the relaxation times are sufficiently long, B_{pp} can be chosen to be smaller than the resonator bandwidth. In this case, there is no timing restriction on τ , but the Φ function in Eq. (13) must be modified with the use of Eq. (5).

Eqs. (6) – (13) were derived under the assumption that the pulse lengths are much shorter than the delay, τ , so that the phase gain during the pulse is negligibly small. To justify this simplification, one must recall that the pulses are symmetrically-centered with respect to the zero-crossing, as in Fig. 1. The negative phase gain for $B_z < 0$ cancels positive gain for $B_z > 0$. In addition, one must consider the magnetic field changing during the pulse from the spin excitation standpoint. In the accelerating frame, changes in magnetic field becomes changes in frequency, and constant frequency pulses become chirp pulses. Although spin echoes have been observed using chirp pulses, the experiment is restricted to certain pulse patterns. For very wide scans as in Fig. 2, on-zero out-of-phase components are observed as the result of the chirp effect. Echo signal distortions can be neglected if the excitation bandwidth is larger than the magnetic field change (expressed in frequency units) during the pulse:

$$2\pi/(\tau\gamma) > \pi f_m B_{pp} \tau, \quad (16)$$

With $\alpha = \pi/4$, which gives the lowest modulation field rate required for phase cycling and smallest chirping effect, Eq. (16) can be transformed into Eq. (17) to provide an estimate of the upper τ limit:

$$\tau < \frac{\sqrt{2}}{\pi} P \approx 0.45P \quad (17)$$

It follows that a modulation frequency of a few MHz can be safely used in the experiment.

Even though the modulation frequency may be quite large, the modulation period is much smaller than the pulse length by design (see Fig. 1). As a result, the multi-photon resonance phenomenon [21–23] should not be observed in the proposed experiment.

3. Discussion and Conclusions

Recent success of CW RS EPR, which takes advantage of fast sinusoidal modulation to reduce spin system saturation and improve EPR spectrometer sensitivity [24–27], was the inspiration for considering phase cycling in pulsed RS EPR. Efficiency of the method increases with the incident power and scan rate, approaching that of FT EPR for spin probes with long relaxation times. Because CW RS EPR does not produce an echo, it can be considered standard field-modulated CW EPR with enhanced sensitivity. The primary goal of this paper was to explore the possibility of applying rapid-scan methodology to pulsed EPR. The most fundamental 90° - τ - 180° - τ -echo experiment was chosen for this analysis. Theoretical description supported by numerical integration of the Bloch equations for this simple model demonstrated the feasibility of using field modulation for phase cycling. Experimental implementation of the described method, which would require investments in hardware and other resources, was not intended. It is hoped that this paper will generate interest in the magnetic resonance community and initiate further collaborative development of field modulated pulsed EPR spectroscopy and imaging.

EPR spectroscopy is currently being developed primarily along two mainstream directions: (i) field modulated CW and (ii) pulsed EPR. This paper demonstrates that (i) and (ii) may be considered special cases for a more general method, in which all three components of the magnetic field vector (B_{xy} for pulsing and B_z for phase change) play active roles. Compared to Zeeman resolved EPR, the example of spin echo phase cycling shows that this method can be used in very basic EPR experiments.

The suggested method is expected to be used in conjunction with the conventional phase cycling to further suppress unwanted signals. This may be of critical importance for EPR spectroscopy and imaging, where the spin relaxation times are often of the same order as the resonator ring-down time. Since the ring-down signal does not change with the external magnetic field and the echo does, the suggested method is expected to improve signal-to-noise ratios of the observed signals.

The concept of field modulated phase cycling can also be extended to the saturation recovery type of experiments. Of the methods used for FID is using an offset of the CW detection frequency with respect to the excitation pulse frequency [28]. Magnetic field modulation and numerical transformation into the accelerating frame can be used toward the same goal.

Acknowledgments

The support of this work by NIH K25 EB016040, NIH R21 EB022775, and NIH/NIGMS U54GM104942 are gratefully acknowledged. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

The help in editing the manuscript by Dr. Virginia Meyer is greatly appreciated.

References

1. Keeler, J. Understanding NMR spectroscopy. 2. Chichester: Wiley; 2010. p. 511 S
2. Schweiger, A., Jeschke, G. Principles of pulse electron paramagnetic resonance. Oxford: Oxford University Press; 2001.
3. Rengan SK, et al. Magnetic Field-Pulsed Eldor Spectroscopy. *J Magn Reson.* 1979; 33(2):227–240.
4. Hornak JP, Freed JH. ELDOR Spin Echoes and Slow Motion. *Chem Phys Letters.* 1983; 101(2): 115–119.
5. Maresch GG, et al. 2d-Eldor Detection of Magnetization Transfer of Nitroxides in Disordered Solid Polymers. *Chem Phys Letters.* 1992; 193(1–3):134–140.
6. Saalmueller JW, et al. Characterization of the motion of spin probes and spin labels in amorphous polymers with two-dimensional field-step ELDOR. *J Polym Sci Part B-Polymer Physics.* 1996; 34(6):1093–1104.
7. Saalmueller JW, et al. Two-dimensional field-step ELDOR. A method for characterizing the motion of spin probes and spin labels in glassy solids. *J Magn Reson Series A.* 1995; 117(2):193–208.
8. Dzuba SA, Salnikov ES, Kulik LV. CW EPR, echo-detected EPR, and field-step ELDOR study of molecular motions of nitroxides in o-terphenyl glass: Dynamical transition, dynamical heterogeneity and beta-relaxation. *Appl Magn Reson.* 2006; 30(3–4):637–650.
9. Kulik LV, et al. Electron dipole-dipole ESEEM in field-step ELDOR of nitroxide biradicals. *J Magn Reson.* 2002; 157(1):61–8. [PubMed: 12202133]
10. Hyde JS, Chien JCW, Freed JH. Electron–Electron Double Resonance of Free Radicals in Solution. *J Chem Phys.* 1968; 48(9):4211.
11. Tkach I, et al. A dual-mode microwave resonator for double electron-electron spin resonance spectroscopy at W-band microwave frequencies. *J Magn Reson.* 2011; 209(2):341–6. [PubMed: 21333570]
12. Dubinskii AA, et al. Submicrosecond field-jump device for pulsed high-field ELDOR. *Appl Magn Reson.* 2002; 22(3):369–386.
13. Eichel RA, Schweiger A. Electron-Zeeman Resolved Electron Paramagnetic Resonance Spectroscopy. *J Magn Reson.* 2001; 152:276–287.
14. Eichel RA, Schweiger A. Polarization-transfer electron-Zeeman resolved EPR. *Chemical Physics Letters.* 2002; 358(3–4):271–277.
15. Gupta RK, Ferretti JA, Becker ED. Rapid Scan Fourier-Transform Nmr-Spectroscopy. *Journal of Magnetic Resonance.* 1974; 13(3):275–290.
16. Dadok J, Sprecher RF. Correlation Nmr-Spectroscopy. *Journal of Magnetic Resonance.* 1974; 13(2):243–248.
17. Tseitlin M, et al. Deconvolution of sinusoidal rapid EPR scans. *J Magn Reson.* 2011; 208(2):279–83. [PubMed: 21163677]
18. Marsh D. EPR moments for site-directed spin-labelling. *J Magn Reson.* 2014; 248:66–70. [PubMed: 25314083]
19. Griffith OH, Wagoner AS. Nitroxide Free Radicals: Spin Labels for Probing Biomolecular Structure. *Acc Chem Res.* 1969; 2:17–24.
20. Epel B, Halpern HJ. Comparison of pulse sequences for R-based electron paramagnetic resonance oxygen imaging. *J Magn Reson.* 2015; 254:56–61. [PubMed: 25828242]
21. Fedin M, et al. Applications of pi-photon-induced transparency in two-frequency pulse electron paramagnetic resonance experiments. *Journal of Chemical Physics.* 2004; 120(3):1361–1368. [PubMed: 15268261]

22. Kalin M, Gromov I, Schweiger A. Transparency in two-level spin systems induced by a longitudinal field. *Physical Review A*. 2004; 69(3)
23. Gromov I, Schweiger A. Multiphoton resonances in pulse EPR. *Journal of Magnetic Resonance*. 2000; 146(1):110–121. [PubMed: 10968963]
24. Mitchell DG, et al. X-band rapid-scan EPR of nitroxyl radicals. *J Magn Reson*. 2012; 214(1):221–6. [PubMed: 22169156]
25. Mitchell DG, et al. Comparison of Continuous Wave, Spin Echo, and Rapid Scan EPR of Irradiated Fused Quartz. *Radiat Meas*. 2011; 46(9):993–996. [PubMed: 22003310]
26. Mitchell DG, et al. Use of rapid-scan EPR to improve detection sensitivity for spin-trapped radicals. *Biophys J*. 2013; 105(2):338–42. [PubMed: 23870255]
27. Mitchell DG, et al. X-Band Rapid-scan EPR of Samples with Long Electron Relaxation Times: A Comparison of Continuous Wave, Pulse, and Rapid-scan EPR. *Mol Phys*. 2013; 111:2664–2673.
28. Froncisz W, et al. Saturation recovery EPR and ELDOR at W-band for spin labels. *Journal of Magnetic Resonance*. 2008; 193(2):297–304. [PubMed: 18547848]

Fig. 1.

(a) Schematic of a field modulated, two pulse spin echo experiment. 90° and 180° pulses occur at the zero-crossing point of the sinusoidal modulation corresponding to $\theta=0$ and $\theta=\pi$, respectively. The echo signal is formed at $\theta=2\pi$. (b) Evolution of magnetization after 90° pulse (red arrow) that is applied along x-axis of the constant-frequency rotating frame. The magnetization vector, which is along -y following the pulse, evolves under the influence of the modulation to gain an additional phase 2α (blue dashed line). (c) Evolution of magnetization following the 180° pulse (red arrow) is also applied along x-axis. The pulse flips the magnetization vector (solid blue arrow) which evolves to gain -2α phase at the moment of echo.

Figure 2.

Real (solid) and imaginary (dashed) parts of numerical solution of the Bloch equations with $B_{pp} = 9$ G (a) and $B_{pp} = 10$ G (b) which correspond to $\alpha = 4\pi$ and $\alpha = 4\pi + \pi/2$, respectively. 90° , 180° pulses occur at $\theta = 0^\circ$ and 180° , respectively. Echo signal appears at $\theta = 360^\circ$. FID and echo oscillations are caused by the changing precession frequencies of the spins that are under the influence of the sinusoidal modulation. After transformation to the accelerating frame using Eq. (11), (a) becomes (c) and (b) becomes (d). Summation of (c) and (d) eliminates the second FID signal. Relatively small discrepancy in the observed signals for $B_{pp} = 9$ and 10 G (a, b) is transformed into the second FID inversion (c, d). Nonzero out-of-phase (dashed lines) components in (c) and (d) are attributed to the chirp effect discussed below.

Figure 3.

Magnetization evolution from Fig. 1(c and d) after transformation into the accelerating frame of reference. Constant phases of the excitation pulses become time-dependent in the new frame. B_I gains an additional phase -2α in-between the pulses. Phases of FIDs and echoes are described by Eq. (12).

Figure 4.

Plot of phases, Φ , in Eq. (12) (solid line for 2nd FID and dashed line for echo) compared to the results of numerical integration of the Bloch equations. Circular markers represent phase dependence of the second FID. Diamond-shaped markers show echo phase dependence on α .

Figure 5.

Computed signals after transformation into the accelerating frame for $\alpha = -\pi/4$ (a) and $\alpha = \pi/4$ (b) which, when summed, cancel the FID after the second pulse (c). Combination of the standard phase cycling to remove the second FID (d and e) and the field modulation method to suppress the remaining first FID by subtraction of (e) computed with $\alpha = -\pi/8$ from (d) computed with $\alpha = \pi/8$. The result of subtraction is shown in (f).