Supporting Methods Document: detailed description of EPG and isochromat-summation implementations

This document contains supplementary information on the implementations of Extended Phase Graph and isochromat summation simulations featured in the EPG-isochromat project. SPGR and FSE simulations using isochromat summation are implemented in functions `SPGR_isochromat_sim.m` and `FSE_isochromat_sim.m` respectively, while SPGR and FSE simulations using Extended Phase Graphs are implemented in functions `SPGR_EPG_sim.m` and `FSE_EPG_sim.m`. References in this document are given in the text or as footnotes to avoid making a separate bibliography.

1 Isochromat summation: basics

The overall magnetization is described as the average over an ensemble of N isochromats, $\mathbf{M} = \frac{1}{N}\sum_{i=1}^{N}\mathbf{m_i}$. Each individual isochromat magnetization vector $\mathbf{m_i}$ has unit magnitude in thermal equilibrium (i.e. $M_0 = 1$); the dynamics of each can be simulated independently using normal Bloch equation simulation methods. The sequence is simulated as consisting of instantaneous RF induced rotations, followed by periods of relaxation and gradient-induced rotation. Slice selection is ignored.

1.1 RF pulses

The effect of an RF pulse with flip angle θ and phase ϕ is to apply the rotation matrix $\mathbf{R}(\theta,\phi)$ such that $\mathbf{m_i} \rightarrow \mathbf{R}(\theta,\phi)\,\mathbf{m_i}$. In this specific implementation $\mathbf{R}(\theta,\phi)$ is computed from $\mathbf{R}(\alpha,\hat{n})$, a rotation of angle α about arbitrary axis $\hat{n}$:

$$\mathbf{R}(\alpha,\hat{n}) = \begin{bmatrix} \hat{n}_x^2 + \left(1-\hat{n}_x^2\right)\cos\theta & \hat{n}_x\hat{n}_y\left(1-\cos\theta\right) - \hat{n}_z\sin\theta & \hat{n}_x\hat{n}_z\left(1-\cos\theta\right) + \hat{n}_y\sin\theta \\ \hat{n}_x\hat{n}_y\left(1-\cos\theta\right) + \hat{n}_z\sin\theta & \hat{n}_y^2 + \left(1-\hat{n}_y^2\right)\cos\theta & \hat{n}_y\hat{n}_z\left(1-\cos\theta\right) - \hat{n}_x\sin\theta \\ \hat{n}_x\hat{n}_z\left(1-\cos\theta\right) - \hat{n}_y\sin\theta & \hat{n}_y\hat{n}_z\left(1-\cos\theta\right) + \hat{n}_x\sin\theta & \hat{n}_z^2 + \left(1-\hat{n}_z^2\right)\cos\theta \end{bmatrix}$$

The correct rotation is achieved by setting $\alpha = \theta$ and $\hat{n} = \begin{bmatrix}\cos\phi & \sin\phi & 0\end{bmatrix}$. All isochromats experience the same rotation from the RF pulses.

1.2 Free precession

Relaxation effects are included during free precession periods such that $\mathbf{m_i}\left(t+\tau\right) = \mathbf{E}(\tau)\mathbf{m_i}\left(t\right) + \mathbf{e_0}(\tau)$ where $\mathbf{e_0} = \begin{bmatrix} 0 & 0 & 1-E1 \end{bmatrix}^T$ and

$$\mathbf{E} = \begin{bmatrix} E2 & 0 & 0 \\ 0 & E2 & 0 \\ 0 & 0 & E1 \end{bmatrix}$$

with $E1(\tau) = \exp\left\{-\frac{\tau}{T_1}\right\}$ and $E2\left(\tau\right) = \exp\left\{-\frac{\tau}{T_2}\right\}$. As with RF pulses, the relaxation effects apply equally to all isochromats.

Gradient induced dephasing is assumed to be one dimensional, and induces a rotation angle $\psi = -\gamma \int_0^T G(t)\, x\, dt$ - this angle depends on the position of the isochromat, x. Each isochromat has a different ψ and a major subject of this work is investigating the impact of how these angles are chosen. The rotation due to gradient is **specific** to each isochromat and is quantified by rotation matrix $\mathbf{G_i}$:

$$\mathbf{G_i}(\psi_i) = \begin{bmatrix} \cos\psi_i & \sin\psi_i & 0 \\ -\sin\psi_i & \cos\psi_i & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

Note that $\mathbf{G_i}$ and $\mathbf{E}$ commute so they can be applied in any order.

2 Extended Phase Graphs

An introduction to EPG theory is beyond the scope of this document, instead we give details specific to the implementations used in this work. We consider sequences with some minimal time step τ - this could be the TR but could also be any time increment. We will consider regular sequences that have the same net gradient area per time increment. In this case, the magnetization can be described using integer-indexed configuration states $\tilde{F}_n$ for transverse magnetization and $\tilde{Z}_n$ for longitudinal magnetization. Magnetization exists in differing amounts in each of these configurations; the numerical values of $\tilde{F}_n$ and $\tilde{Z}_n$ are sometimes referred to as 'populations' but here we refer to these as 'coefficient values'.

The code treats the magnetization state at any given time point as a column vector $\mathbf{F} = \left[\tilde{F}_0 \tilde{Z}_0 \tilde{F}_1 \tilde{F}_{-1} \tilde{Z}_1 \tilde{F}_2 \tilde{F}_{-2} \tilde{Z}_2 \ldots\right]^T$. The matrices represent the temporal evolution of the magnetization by concatenating these vectors.

Note that in this implementation we apply complex conjugation when states transition from having a positive to negative index and vice-versa: this is discussed in detail by Weigel[1].

[1] Weigel, M. Extended phase graphs: Dephasing, RF pulses, and echoes - pure and simple. J. Magn. Reson. Imaging 41, 266295 (2015).

2.1 RF pulses

The effect of an RF pulse with flip angle θ and phase ϕ is to mix coefficient values of states **with the same n**. This is achieved by applying the 3×3 matrix $\mathbf{T}$ to each set of coefficients $\left[\tilde{F}_n \tilde{F}_{-n} \tilde{Z}_n\right]^T$ in turn:

$$\mathbf{T}(\theta, \phi) = \begin{bmatrix} \cos^2 \frac{\theta}{2} & e^{2i\phi} \sin^2 \frac{\theta}{2} & -ie^{i\phi} \sin\theta \\ e^{-2i\phi} \sin^2 \frac{\theta}{2} & \cos^2 \frac{\theta}{2} & ie^{-i\phi} \sin\theta \\ -\frac{i}{2} e^{-i\phi} \sin\theta & \frac{i}{2} e^{i\phi} \sin\theta & \cos\theta \end{bmatrix}$$

2.2 Free precession

Relaxation effects are included using the same operators as with isochromat summation. Matrix $\mathbf{E}$ as defined above is applied to each set of states $\left[\tilde{F}_n \tilde{F}_{-n} \tilde{Z}_n\right]^T$. The main difference from isochromat summation is in the recovery of magnetization toward thermal equilibrium, modelled by the addition of vector $\mathbf{e_0}$ in isochromat summation. In the EPG picture, recovering magnetization has not been subject to any gradients, hence this term is only applied to $\tilde{Z}_0$.

Gradient induced dephasing is represented by shifts of states: this means that coefficient values are transferred from one state to another. In this implementation we make the assumption that the shift applied at each time increment τ is the same. After each period τ the transverse states are each shifted such that $\tilde{F}_n(t) \rightarrow \tilde{F}_{n+1}(t+\tau)$, while longitudinal states are **not** shifted, i.e. $\tilde{Z}_n(t) \rightarrow \tilde{Z}_n(t+\tau)$. Shifts are efficiently implemented by using a globally defined shift matrix $\mathbf{S}$ applying to the whole state vector.

3 Diffusion effects

3.1 Isochromat summation

Diffusion effects have been implemented as by Gudbjartsson and Patz [2] who discussed inclusion of diffusion as a spatial convolution with kernel ζ:

$$\zeta(x, G, \tau) = \frac{1}{\sqrt{4\pi D\tau}} \exp\left\{\frac{-x^2}{4D\tau} + \frac{i\gamma G x \tau}{2} - \frac{\gamma^2 G^3 D \tau^3}{12}\right\}$$

where G is a constant gradient applied in direction x for time τ and D is the diffusion coefficient. Since the current work didn't include an explicit spatial dimension, this equation was adapted to relate to dephasing angles ψ by using the relationship $\psi = -\gamma G \tau x$, hence $x = -\frac{\psi}{\gamma G \tau}$. Substituting this into the expression for ζ gives

[2] Gudbjartsson, H. & Patz, S. Simultaneous Calculation of Flow and Diffusion Sensitivity in Steady-State Free Precession Imaging. Magn. Reson. Med. 34, 567579 (1995).

$$\zeta(\psi, G, \tau) = \frac{2\pi}{N}\frac{1}{\sqrt{4\pi D\tau}}\exp\left\{\frac{-\psi^2}{4D\gamma^2G^2\tau^3} - \frac{i\psi}{2} - \frac{\gamma^2G^3D\tau^3}{12}\right\}$$

Here the factor $\frac{2\pi}{N}$ has been introduced because of the discrete sampling of ψ (see Yarnykh[3]). While this kernel is applied to the transverse magnetization, the kernel for blurring of longitudinal magnetization is given by just the first term in the exponential. We have followed the treatment by Gudbjartsson and Patz in implementing this convolution as a multiplication in the Fourier domain. The convolution is applied during the free precession period of the simulation.

3.2 EPG

Diffusion effects in EPG are well described by Weigel[4]. The effect of simple isotropic diffusion is to introduce an additional matrix $\mathbf{D}$ to apply alongside $\mathbf{E}$ during the free precession period.

$$\mathbf{D} = \begin{bmatrix} D^T & 0 & 0 \\ 0 & D^T & 0 \\ 0 & 0 & D^L \end{bmatrix}$$

where $D^T = \exp\left(-b^T D\right)$ and $D^L = \exp\left(-b^L D\right)$: D is the diffusion coefficient and b^T/b^L are b-values of the applied gradient corresponding to transverse/longitudinal components of the magnetization. $\mathbf{D}$ is a diagonal matrix and acts in a similar way to $\mathbf{E}$ except that its values are dependent on the k-space position (i.e. variable as a function of n). The b-values for a constant gradient applied for duration τ are:

$$b^T = \frac{\tau}{3}\left(k_i^2 + k_f^2 + k_i k_f\right)$$
$$b^L = k_i^2\tau$$

where k_i and k_f are the k-space positions at the beginning and end of the gradient under consideration . It is possible to use this logic to compute b-values for time-variable gradients by integrating over smaller time periods. This is implemented in the helper function `bfactors` within the SPGR implementations.

For a single period τ of constant gradient G, the $k_i = n\Delta k$ and $k_f = (n+1)\Delta k$, where $\Delta k = \gamma G\tau$ is the k-space increment from the application of this gradient and n is the index of the configuration state this b-value applies

[3] Yarnykh, V. L. Optimal radiofrequency and gradient spoiling for improved accuracy of T1 and B1 measurements using fast steady-state techniques. Magn. Reson. Med. 63, 161026 (2010).

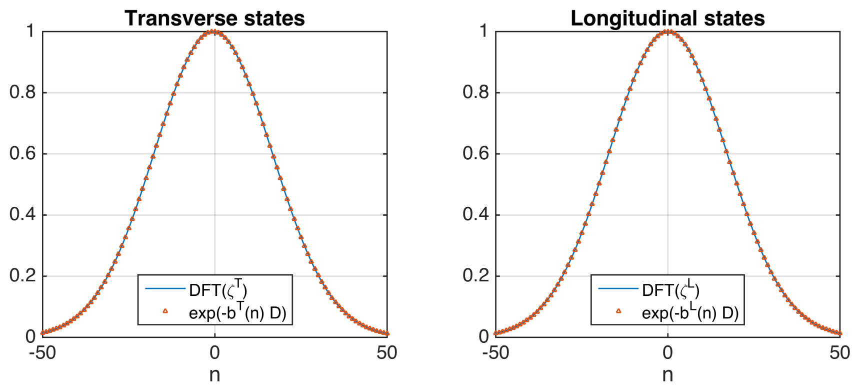
[4] Weigel, M., Schwenk, S., Kiselev, V. G., Scheffler, K. & Hennig, J. Extended phase graphs with anisotropic diffusion. J. Magn. Reson. 205, 27685 (2010).

to. Hence

$$b^T(n) = \gamma^2 G^2 \tau^3 \left(n^2 + n + \frac{1}{3}\right)$$
$$b^L(n) = \gamma^2 G^2 \tau^3 n^2$$

3.3 Comparison of diffusion in EPG and isochromat domain

The EPG and isochromat domain representations of diffusion have previously been shown to be equivalent (for example see Weigel[4]). To confirm this we implemented both of the above for the (arbitrary) example G=10 mT/m, τ=2ms and $D = 3 \times 10^{-9} m^2/s$. To make a comparison we computed the magnitude of the filter in the k-space (EPG) domain, either directly from the expressions for $D^T(n)$ and $D^L(n)$ developed above for EPG, or indirectly by taking the DFT of ζ.



Supporting Methods Figure 1: Comparison of k-space filter representing diffusion ($k = n\Delta k$) when computed using the EPG or isochromat based formalisms

The plots (Supplement Methods Figure 1) show that there is a close correspondence between both methods, as expected. Hence in this work we have implemented the diffusion using the **same** convolution kernels for EPG and isochromat summation. In the EPG calculation the kernels are applied multiplicatively via matrix operator **D**; in the isochromat summation calculations they are also applied multiplicatively after a DFT on the isochromat distribution, as originally proposed by Gudbjartsson and Patz.

4 Specific Sequence implementations

4.1 Spoiled Gradient Echo (SPGR)

The SPGR sequence is modelled straightforwardly as repeating blocks of RF pulse followed by free precession for period TR (RF pulses are assumed instantaneous). Relaxation and diffusion effects are assumed to occur for time TR. The state of magnetization directly after each RF pulse is recorded.

4.1.1 Isochromat Summation

Implemented in `SPGR_isochromat_sim.m`. $\mathbf{m_i}(p)$ is the isochromat magnetization vector immediately after the p^{th} RF pulse. The next is obtained using the following steps in this order:

$$\mathbf{m_i}(p+1) = \mathbf{R}\left\{\mathbf{E}\mathbf{G_i}\mathbf{m_i}(p) + \mathbf{e_0}\right\}$$

where the RF pulse phase is cycled as described in the paper.

If diffusion is included the isochromats are no longer independent of one another. Instead forward ($\mathbf{\Lambda}$) and inverse ($\mathbf{\Lambda}^{-1}$) DFTs are added over the whole ensemble. Filters D^T and D^L are applied to the transverse and longitudinal components, respectively - denote this filtering step as multiplication by filter D_f:

$$\mathbf{m_i}(p+1) = \mathbf{R}\mathbf{\Lambda}^{-1}D_f\mathbf{\Lambda}\left\{\mathbf{E}\mathbf{G_i}\mathbf{m_i}(p) + \mathbf{e_0}\right\}$$

i.e. diffusion is applied after relaxation.

4.1.2 EPG

Implemented in `SPGR_EPG_sim.m`. The state vector $\mathbf{F}(p)$ records the state immediately following the p^{th} RF pulse. The next one is computed by the following steps:

$$\mathbf{F}(p+1) = \mathbf{A}\mathbf{S}\left\{\mathbf{E}\mathbf{D}\mathbf{F}(p) + \mathbf{e_0}\right\}$$

Here $\mathbf{E}$ and $\mathbf{D}$ commute, however the latter depends on the index of the state. Note that although this could be implemented using large block diagonal matrices, instead the steps are separately implemented for each subgroup $\mathbf{F}_n = \left[\tilde{F}_n \tilde{F}_{-n} \tilde{Z}_n\right]^T$ by looping since this was actually found to be more efficient. Note also that $\mathbf{e_0}$ is added only to the $\tilde{Z}_0$ state and complex conjugation is applied for transitions from negative to positive n, as described above.

4.2 Fast Spin Echo (FSE)

FSE is a little more complicated since we have an initial delay period τ after the excitation pulse, followed by periods 2τ between each refocusing pulse. The signal is recorded at the echo time which is τ after each refocusing pulse. All relaxation operators are calculated for time τ, diffusion was not implemented for FSE..

4.2.1 Isochromat Summation

Implemented in `FSE_isochromat_sim.m`. $\mathbf{m_i}(p)$ is the isochromat magnetization vector at the time of the p^{th} echo. The next is obtained using the following steps in this order:

$$\mathbf{m_i}(p+1) = \{\mathbf{EG_iR}_p\,\{\mathbf{EG_im_i}(p) + \mathbf{e_0}\}\} + \mathbf{e_0}$$

where $\mathbf{R}_p$ is the rotation associated with the p^{th} refocusing pulse. $\mathbf{G}_i$ is the net gradient induced rotation between excitation and refocusing pulses. Note that $\mathbf{G}_i$ and relaxation matrices are applied twice between each refocusing pulse. The period between the excitation pulse and first refocusing pulse is dealt with separately with only one period τ as appropriate. All operations are performed using large block diagonal matrices.

4.2.2 EPG

Implemented in `FSE_EPG_sim.m`. The state vector $\mathbf{F}(p)$ records the state at the time of the p^{th} echo. The next one is computed as follows:

$$\mathbf{F}(p+1) = \mathbf{SE}\,\{\mathbf{A}_p\,\{\mathbf{SEF}(p) + \mathbf{e_0}\}\} + \mathbf{e_0}$$

where $\mathbf{A}_p$ is the RF transition matrix associated with the p^{th} refocusing pulse and $\mathbf{S}$ is the shift matrix for the gradient between excitation and first refocusing pulse (i.e. half the gradient between each echo). All operations were performed using large single matrix multiplications. As with the isochromat implementation, relaxation effects are considered twice, once after each refocusing pulse and before the echo, and once after the echo and before the next refocusing pulse.

5 Conclusion

This document explains how each sequence was implemented using each method. The results in the paper demonstrate that when implemented in this way the EPG and isochromat summation simulations are exactly equivalent. Please see the code for more details.