Advances in Quantitative MRI: Acquisition, Estimation, and Applications

by

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ABSTRACT

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We show that it is possible to get approximate solutions to analytically intractable equations using iterative methods. Thus we show that the author could pass an undergraduate class in numerical analysis. In addition, a unique extension to Brent's method is proposed that results in slight improvements in convergence.

CHAPTER 1

Introduction

Magnetic resonance imaging (MRI) is a non-invasive tool that has earned widespread clinical adoption due (among other factors) to its potential for excellent soft tissue contrast, its avoidance of ionizing radiation, and its flexibility to characterize many physical phenomena. Despite its numerous advantages, MRI requires highly specialized hardware, ongoing liquid-helium cooling of its superconducting main magnet, and comparably long scan times. For these reasons, MRI is (somewhat inherently) expensive relative to other medical imaging modalities. Accordingly, one broad initiative recently advocated by the MR community is to increase the *value* of MRI examinations.

Two reasonable measures of an acquisition's value are its sensitivity to a given disorder and its specificity in distinguishing it from others. The field of *pathology* seeks to ascribe physical processes to disorders of interest with high sensitivity and specificity. The field of *quantitative MRI* (QMRI) seeks to build MRI biomarkers that measurably describe such physical processes and thereby provide indirect information about the onset and progression of underlying conditions.

QMRI poses several challenges beyond those of commonplace anatomical MRI and thus remains yet to be widely adopted clinically. For example, latent parameter "maps" that describe relevant physical processes are often related to the received MR signal through complicated, highly nonlinear relationships. Furthermore, practical MR pulse sequences produce signals that are usually functions of not only desired but also nuisance parameters. Scan repetition is often necessary for accurate estimation of multiple desired and nuisance parameters, which can increase scan times. Mitigating these challenges (and likely others) is essential to furthering widespread clinical adoption of QMRI techniques.

1.1 Thesis Overview

In this thesis, we seek to build a systematic framework towards QMRI. We borrow tools from optimization, statistics, and machine learning to construct time-efficient workflows for quantifiably characterizing physical processes of interest. We apply this framework to challenging QMRI problems that are motivated by pathological studies. Our goal is to introduce tools that aid in identifying clinical tasks for which QMRI should (or should not) be part of a targeted, high-value MRI examination.

We consider two distinct subproblems in our framework. Questions in *acquisition design* (Chapters 4,6) ask how to assemble fast collections of scans that yield data rich in information about physical processes of interest. Questions in *parameter estimation* (Chapters 3,5) ask how to quickly and reliably quantify parameters associated with these relevant physical processes. The overall framework seeks to first design fast and informative scans based on the application, and to then accurately and precisely estimate application-specific parameters of interest.

1.2 Thesis Organization

The main body of this thesis is organized as follows:

- Chapter 2 reviews relevant background MR material about DESS,SPGR,blahblah...

- Chapter 3 discusses methods for MRI parameter estimation from likelihood models and applies these methods for model-based MR relaxometry, (*i.e.*, estimation of relaxation parameters T_1, T_2), of interest for many neurological applications. It derives some content (especially regarding applications) from conference papers [1, 2].

- Chapter 4 introduces a minimax optimization approach to aid robust and application-specific MR scan selection and optimization for precise latent parameter estimation. It optimizes several practical acquisitions and uses the likelihood-based estimation techniques introduced in Chapter 3 to assess the utility of scan optimization through simulations, phantom studies, and *in vivo* experiments. It derives content mainly from journal paper [3] and conference paper [4].

- Chapter 5 describes MRI parameter estimation using kernel ridge regression. It derives content from conference paper [5].

- Chapter 6 introduces a multi-compartmental model for relevant MR pulse sequences and proposes a new acquisition useful for myelin water fraction estimation, of in-

terest in white matter disorders. It applies kernel-based MR parameter estimation to estimate myelin water fraction, in simulations and *in vivo* experiments. It derives some content from conference paper [6].

- Chapter 7 presents some relatively immature ideas on steady-state radiofrequency (RF) pulse design as well as associated challenges. This work is presently unpublished and may offer avenues for further research.

- Chapter 8 summarizes several items of possible future work (on both short- and long-term timescales) and presents a timeline for completion of this thesis.

The appendices are organized as follows:

- Appendix A proposes an algorithm for combining multiple MRI datasets (as is necessary for many parameter estimation problems), when each dataset is acquired using multiple receiver coils.

- Appendix B presents an analysis of DESS in the presence of diffusion, shows that neglecting diffusive effects during T_2 estimation from DESS can cause significant bias, and suggests acquisition modifications for mitigating this bias.

CHAPTER 2

Background

This chapter focuses only on background information pertinent to multiple subsequent chapters. We present further topic-specific information at the beginnings of corresponding chapters. Section 2.1 places emphasis on reviewing necessary MR fundamentals, and Section 2.2 proceeds to a shorter discussion regarding optimization as it pertains to QMRI.

2.1 Relevant MR Physics

This section begins with the fundamental Bloch equations and derives the signal models associated with two MR pulse sequences used extensively in this thesis. Our coverage of MRI is far from comprehensive, and omits fundamental but tangential topics such as signal localization. We refer the interested reader to books such as [7, 8, 9].

2.1.1 Bloch Equations

The Bloch equations [10] describe the magnetization dynamics of *spins*, or (loosely) atomic nuclei with nonzero angular momentum and thus nonzero magnetic moment, *e.g.* ^{1}H. If the dominant source of magnetic flux arises (as is typical in MRI) from a main magnetic field that is oriented along the z-axis, the equations read

$$\frac{\partial}{\partial t}m_{xy}(\mathbf{r},t) = i\gamma(m_z(\mathbf{r},t)b_{xy}(\mathbf{r},t) - m_{xy}(\mathbf{r},t)b_z(\mathbf{r},t)) - \frac{m_{xy}(\mathbf{r},t)}{T_2(\mathbf{r})}; \qquad (2.1)$$

$$\frac{\partial}{\partial t}m_z(\mathbf{r},t) = \gamma(m_x(\mathbf{r},t)b_y(\mathbf{r},t) - m_y(\mathbf{r},t)b_x(\mathbf{r},t)) - \frac{m_z(\mathbf{r},t) - m_0(\mathbf{r})}{T_1(\mathbf{r})}. \qquad (2.2)$$

Here, $m_{xy}(\mathbf{r},t) := m_x(\mathbf{r},t) + im_y(\mathbf{r},t) \in \mathbb{C}$ and $m_z(\mathbf{r},t) \in \mathbb{R}$ are the transverse and longitudinal components of the magnetization vector at position $\mathbf{r} \in \mathbb{R}^3$ and time $t \geq 0$; $b_{xy}(\mathbf{r},t) := b_x(\mathbf{r},t) + ib_y(\mathbf{r},t) \in \mathbb{C}$ and $b_z(\mathbf{r},t) \in \mathbb{R}$ are the transverse and longitudinal components (in an inertial reference frame) of the applied magnetic field; $T_1(\mathbf{r})$ and $T_2(\mathbf{r})$

are spin-lattice and spin-spin relaxation time constants; $m_0(\mathbf{r})$ is the equilibrium magnetization and is proportional to the density of spins per unit volume as well as the main field strength; γ is the gyromagnetic ratio; and $i := \sqrt{-1}$. As written, equations (2.1)-(2.2) only model dominant temporal dynamics; later chapters consider second-order effects such as multiple magnetization compartments (Chapter 6) and diffusion (Appendix B).

It is often convenient to study Bloch dynamics in a non-inertial reference frame rotating clockwise about the z-axis at Larmor frequency $\omega_0 := \gamma B_0$, where $B_0 \hat{k}$ is the (nearly uniform) main magnetic field. In these coordinates, the apparent transverse magnetic field $b'_{xy}(\mathbf{r}, t) = b'_x(\mathbf{r}, t) + i b'_y(\mathbf{r}, t) := b_{xy}(\mathbf{r}, t) e^{i\omega_0 t}$ transforms only in phase, but the apparent longitudinal magnetic field $b'_z(\mathbf{r}, t) := b_z(\mathbf{r}, t) - B_0$ is greatly reduced in magnitude. The magnetization components transform more simply as $m'_{xy}(\mathbf{r}, t) = m'_x(\mathbf{r}, t) + i m'_y(\mathbf{r}, t) := m_{xy}(\mathbf{r}, t) e^{i\omega_0 t}$ and $m'_z(\mathbf{r}, t) := m_z(\mathbf{r}, t)$. Remarkably, inserting these coordinate transformations into (2.1)-(2.2) does not change the form of the dynamical equations:

{eq:bloch-mxyp}
$$\frac{\partial}{\partial t} m'_{xy}(\mathbf{r}, t) = i\gamma \left(m'_z(\mathbf{r}, t) b'_{xy}(\mathbf{r}, t) - m'_{xy}(\mathbf{r}, t) b'_z(\mathbf{r}, t) \right) - \frac{m'_{xy}(\mathbf{r}, t)}{T_2(\mathbf{r})}; \tag{2.3}$$

{eq:bloch-mzp}
$$\frac{\partial}{\partial t} m'_z(\mathbf{r}, t) = \gamma \left(m'_x(\mathbf{r}, t) b'_y(\mathbf{r}, t) - m'_y(\mathbf{r}, t) b'_x(\mathbf{r}, t) \right) - \frac{m'_z(\mathbf{r}, t) - m_0(\mathbf{r})}{T_1(\mathbf{r})}. \tag{2.4}$$

It thus suffices to consider how perturbations $\mathbf{b}'(\mathbf{r}, t)$ to main field $B_0 \hat{k}$ influence rotating-frame magnetization $\mathbf{m}'(\mathbf{r}, t)$ via Eqs. (2.3)-(2.4). The inertial-frame magnetization $\mathbf{m}(\mathbf{r}, t)$ is then easily constructed via $m_{xy}(\mathbf{r}, t) = m'_{xy}(\mathbf{r}, t) e^{-i\omega_0 t}$ and $m_z(\mathbf{r}, t) = m'_z(\mathbf{r}, t)$.

It is challenging to explicitly solve Eqs. (2.3)-(2.4) for arbitrary field perturbations $\mathbf{b}'(\mathbf{r}, t)$. We discuss relevant special cases in the following.

2.1.1.1 Non-Selective Excitation

{sss,bkgrd,mri,bloch,ex}

Here, we derive solutions to Eqs. (2.3)-(2.4) in the case of short, spatially non-selective excitations. We take the following common assumptions:

- We assume negligible spatial variation in the longitudinal magnetic field, so $b'_z(\mathbf{r}, t) \approx 0$. This lack of spatial variation is reason for non-selective excitation.

- We assume the transverse field separates in position and time; oscillates at the Larmor frequency (commonly in the radiofrequency (RF) range); and aligns at initial time $t \leftarrow t_0$ with the x-axis. Together, these assumptions restrict the so-called RF excitation to take form $b'_{xy}(\mathbf{r}, t) \approx s^{\mathrm{t}}(\mathbf{r}) b'_{1,x}(t) \hat{i} + 0 \hat{j}$, where $s^{\mathrm{t}}(\mathbf{r}) \in \mathbb{R}$ is the RF transmit coil spatial variation and $b'_{1,x}(t) \in \mathbb{R}$ is the RF excitation envelope.

- We assume that the duration T_P of RF excitation (often $T_\mathrm{P} \sim 1$ms) is much shorter than relaxation time constants (typically $T_1 \sim 1000$ms and $T_2 \sim 50$ms in brain tissue) and thus neglect relaxation effects during excitation.

Under these assumptions, Eqs. (2.3)-(2.4) reduce to the linear system

{eq:bloch-rot}
$$\frac{\partial}{\partial t} \begin{bmatrix} m'_x(\mathbf{r}, t) \\ m'_y(\mathbf{r}, t) \\ m'_z(\mathbf{r}, t) \end{bmatrix} = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & \gamma s^\mathrm{t}(\mathbf{r}) b'_{1,x}(t) \\ 0 & -\gamma s^\mathrm{t}(\mathbf{r}) b'_{1,x}(t) & 0 \end{bmatrix} \begin{bmatrix} m'_x(\mathbf{r}, t) \\ m'_y(\mathbf{r}, t) \\ m'_z(\mathbf{r}, t) \end{bmatrix}. \tag{2.5}$$

Eq. (2.5) admits the simple solution (for $t \geq t_0$)

{eq:rot-sol}
$$\begin{bmatrix} m'_x(\mathbf{r}, t) \\ m'_y(\mathbf{r}, t) \\ m'_z(\mathbf{r}, t) \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos(\alpha(\mathbf{r}, t; t_0)) & \sin(\alpha(\mathbf{r}, t; t_0)) \\ 0 & -\sin(\alpha(\mathbf{r}, t; t_0)) & \cos(\alpha(\mathbf{r}, t; t_0)) \end{bmatrix} \begin{bmatrix} m'_x(\mathbf{r}, t_0) \\ m'_y(\mathbf{r}, t_0) \\ m'_z(\mathbf{r}, t_0) \end{bmatrix}, \tag{2.6}$$

where $\mathbf{m}'(\mathbf{r}, t_0) := \left[m'_x(\mathbf{r}, t_0), m'_y(\mathbf{r}, t_0), m'_z(\mathbf{r}, t_0) \right]^\mathsf{T}$ is the initial magnetization and

{eq:flip-def}
$$\alpha(\mathbf{r}, t; t_0) := \gamma s^\mathrm{t}(\mathbf{r}) \int_{t_0}^{t} b'_{1,x}(\tau) \, \mathrm{d}\tau \tag{2.7}$$

is the nutation (or "flip") angle at time t. Eq. (2.6) reveals that on-resonance RF excitation causes the magnetization vector to rotate clockwise about an axis parallel to the direction of excitation. The nutation angle accumulated over an RF pulse of duration T_P is often decomposed as $\alpha(\mathbf{r}, t_0 + T_\mathrm{P}; t_0) =: \alpha_0 s^\mathrm{t}(\mathbf{r})$, where α_0 is a prescribed nominal flip angle.

For deriving signal models in later sections, it is convenient and intuitive to define matrix operators that summarize relevant dynamics. Here, we rewrite Eq. (2.6) as

{eq:mtx-ex}
$$\mathbf{m}'(\mathbf{r}, t) = \mathbf{R}_{x'}(\alpha(\mathbf{r}, t; t_0))\mathbf{m}'(\mathbf{r}, t_0), \tag{2.8}$$

where $\mathbf{R}_{x'}(\alpha(\mathbf{r}, t; t_0))$ denotes a clockwise rotation of angle $\alpha(\mathbf{r}, t; t_0)$ about the x'-axis.

2.1.1.2 Free Precession and Relaxation

{sss,bkgrd,mri,bloch,pr}

Next, we derive solutions to the rotating-frame Bloch equations when no RF excitation is present, *i.e.* $b'_{xy}(\mathbf{r}, t) \approx 0$. In this case, Eqs. (2.3)-(2.4) decouple, yielding separate

dynamical equations for the transverse and longitudinal magnetization components:

$$\{eq:bloch\text{-}free\text{-}mxyp\} \qquad \frac{\partial}{\partial t}m'_{xy}(\mathbf{r}, t) = -i\gamma m'_{xy}(\mathbf{r}, t)b'_z(\mathbf{r}, t) - \frac{m'_{xy}(\mathbf{r}, t)}{T_2(\mathbf{r})}; \qquad (2.9)$$

$$\{eq:bloch\text{-}free\text{-}mzp\} \qquad \frac{\partial}{\partial t}m'_z(\mathbf{r}, t) = -\frac{m'_z(\mathbf{r}, t) - m_0(\mathbf{r})}{T_1(\mathbf{r})}. \qquad (2.10)$$

Eqs. (2.9)-(2.10) admit simple solutions with no further assumptions:

$$\{eq:mxy\text{-}fp\} \qquad m'_{xy}(\mathbf{r}, t) = m'_{xy}(\mathbf{r}, t_0)e^{-(t-t_0)/T_2(\mathbf{r})}e^{-i\phi'(\mathbf{r}, t; t_0)}; \qquad (2.11)$$

$$\{eq:mz\text{-}fp\} \qquad m'_z(\mathbf{r}, t) = m'_z(\mathbf{r}, t_0)e^{-(t-t_0)/T_1(\mathbf{r})} + m_0(\mathbf{r})\big(1 - e^{-(t-t_0)/T_1(\mathbf{r})}\big), \qquad (2.12)$$

where $m'_{xy}(\mathbf{r}, t_0)$ and $m'_z(\mathbf{r}, t_0)$ are the initial magnetization components and

$$\{eq:ph\text{-}def\} \qquad \phi'(\mathbf{r}, t; t_0) := \gamma \int_{t_0}^{t} b'_z(\mathbf{r}, \tau)\,\mathrm{d}\tau \qquad (2.13)$$

denotes the phase accumulation due to main field inhomogeneity (often called off-resonance effects). Eq. (2.11) reveals that without RF excitations, the transverse magnetization $m'_{xy}(\mathbf{r}, t)$ relaxes to zero exponentially fast with time constant $T_2(\mathbf{r})$, while accruing phase due to off-resonance effects. Eq. (2.12) similarly reveals that without RF excitations, longitudinal magnetization $m'_z(\mathbf{r}, t)$ recovers to $m_0(\mathbf{r})$ exponentially fast with time constant $T_1(\mathbf{r})$.

As in Section 2.1.1.2, we rewrite Eqs. (2.11)-(2.12) for $t \geq t_0$ using matrix operators:

$$\{eq:mtx\text{-}pr\} \qquad \mathbf{m}'(\mathbf{r}, t) = \mathbf{R}_{z'}(\phi'(\mathbf{r}, t; t_0))\mathbf{E}(\mathbf{r}, t; t_0)\mathbf{m}'(\mathbf{r}, t_0) + \mathbf{m}_0(\mathbf{r}, t; t_0) \qquad (2.14)$$

where $\mathbf{m}_0(\mathbf{r}, t; t_0) := m_0(\mathbf{r})\big(1 - e^{-(t-t_0)/T_1(\mathbf{r})}\big)\hat{k}$;

$$\{eq:op\text{-}rotz\} \qquad \mathbf{R}_{z'}(\phi'(\mathbf{r}, t; t_0)) := \begin{bmatrix} \cos\left(\phi'(\mathbf{r}, t; t_0)\right) & \sin\left(\phi'(\mathbf{r}, t; t_0)\right) & 0 \\ -\sin\left(\phi'(\mathbf{r}, t; t_0)\right) & \cos\left(\phi'(\mathbf{r}, t; t_0)\right) & 0 \\ 0 & 0 & 1 \end{bmatrix} \qquad (2.15)$$

denotes a clockwise rotation of angle $\phi'(\mathbf{r}, t; t_0)$ about the z'-axis; and

$$\{eq:op\text{-}relax\} \qquad \mathbf{E}(\mathbf{r}, t; t_0) := \begin{bmatrix} e^{-(t-t_0)/T_2(\mathbf{r})} & 0 & 0 \\ 0 & e^{-(t-t_0)/T_2(\mathbf{r})} & 0 \\ 0 & 0 & e^{-(t-t_0)/T_1(\mathbf{r})} \end{bmatrix} \qquad (2.16)$$

is an exponential relaxation operator. Section 2.1.2 (and later chapters) use matrix dynamical representations (2.8) and (2.14) to succinctly describe pulse sequence signal models.

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2.1.2 Steady-State Sequences

MRI experiments typically involve repeated cycles of (pulsed) RF excitation; signal localization (not discussed here); and transverse T_2 relaxation and free precession, alongside (relatively slow) longitudinal T_1 recovery. We can build models of the received MR signal by considering the magnetization dynamics induced by specific pulse sequences.

Classical pulse sequences use relatively long cycle repetition times T_R to ensure near-complete T_1 recovery of the magnetization vector back to equilibrium state $m_0(\mathbf{r})\hat{k}$ prior to the start of each RF cycle. For such long-T_R sequences, it suffices to approximate the magnetization as fully recovered (*i.e.*, $\mathbf{m}'(\mathbf{r}, t_0 + rT_R) \approx m_0(\mathbf{r})\hat{k}, \forall r \in \{0, 1, 2, \dots\}$) just prior to each RF excitation. This approximation yields a sequence of initial conditions and allows computation of the magnetization at corresponding times of data acquisition via direct application of Bloch dynamics (2.8) and (2.14). Resulting signal models are typically simple expressions of relaxation parameters $T_1(\mathbf{r})$ and $T_2(\mathbf{r})$; however, model accuracy often depends strongly on the long-T_R assumption, which requires long acquisitions.

Steady-state (SS) sequences [11] utilize short T_R, and can thus achieve much faster scan times. Due to short repetition times, SS sequences achieve only partial T_1 recovery in between RF excitations; thus, their magnetization responses do not obey the simple classical initial conditions (for the second RF cycle onwards). Although their transient magnetization dynamics can be complicated, SS sequences produce (under certain assumptions [12]) long-time magnetization responses that eventually[1] achieve a steady-state condition:

$$\lim_{t_0 \to \infty} \mathbf{m}'(\mathbf{r}, t_0 + rT_R) = \mathbf{m}'(\mathbf{r}, t_0), \tag{2.17}$$

where repetition count $r \in \{1, 2, \dots\}$ for fixed RF excitations and off-resonance induced phase increments (as is assumed in the following). Subsections 2.1.2.1 and 2.1.2.2 use SS condition (2.17) and Bloch equation matrix operators introduced in (2.8) and (2.14) to derive long-time signal models for Spoiled Gradient-Recalled Echo (SPGR) and Dual-Echo Steady-State (DESS), two SS pulse sequences useful for quantitative MRI.

2.1.2.1 Spoiled Gradient-Recalled Echo (SPGR) Sequence

SPGR [14] is a fast pulse sequence that repeats cycles of fixed RF excitation (such that $b'_{1,x}(t + rT_R) = b'_{1,x}(t), \forall t \in [t_0, t_0 + T_P], r \in \{1, 2, \dots\}$); data acquisition; relaxation and recovery; and residual transverse magnetization "spoiling" (discussed later). Here we

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[1]The progression to steady state takes on the order of $5T_2/T_R$ RF cycles [12], typically a small but not insignificant period during which data acquisition is often foregone. This transition can (in some cases) be accelerated by prepending SS sequences with tailored "magnetization-catalyzing" modules [13].

develop a simple and popular steady-state SPGR signal model.

Let $\mathbf{m}'(\mathbf{r}, t_0)$ denote the magnetization at an initial time t_0 selected well into the steady-state and just prior to excitation. The SPGR sequence first applies an RF excitation, which rotates the initial magnetization as per (2.8):

$$\mathbf{m}'(\mathbf{r}, t_0 + T_\mathrm{P}) = \mathbf{R}_{x'}(\alpha(\mathbf{r}, t_0 + T_\mathrm{P}; t_0))\mathbf{m}'(\mathbf{r}, t_0). \tag{2.18}$$

The excited magnetization then precesses and relaxes as per (2.14) until data acquisition, defined to occur at "echo time" $T_\mathrm{E} \in [T_\mathrm{P}, T_\mathrm{R}]$ after the (midpoint of) RF excitation:

$$\mathbf{m}'\left(\mathbf{r}, t_0 + \frac{T_\mathrm{P}}{2} + T_\mathrm{E}\right) = \mathbf{R}_{z'}\left(\phi'\left(\mathbf{r}, \frac{T_\mathrm{P}}{2} + T_\mathrm{E}; T_\mathrm{P}\right)\right)\mathbf{E}\left(\mathbf{r}, \frac{T_\mathrm{P}}{2} + T_\mathrm{E}; T_\mathrm{P}\right)\mathbf{m}'(\mathbf{r}, t_0 + T_\mathrm{P})$$

$$+ \mathbf{m}_0\left(\mathbf{r}, \frac{T_\mathrm{P}}{2} + T_\mathrm{E}; T_\mathrm{P}\right). \tag{2.19}$$

Following signal reception, the remaining transverse magnetization is spoiled[2] while the longitudinal component is unaffected. We model an ideal spoiling operation as

$$\mathbf{S}\mathbf{m}'\left(\mathbf{r}, \frac{T_\mathrm{P}}{2} + T_\mathrm{E}\right), \quad \text{where} \quad \mathbf{S} := \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 1 \end{bmatrix}. \tag{2.20}$$

After spoiling, the longitudinal magnetization (partially) recovers until $t \leftarrow t_0 + T_\mathrm{R}$:

$$\mathbf{m}'(\mathbf{r}, t_0 + T_\mathrm{R}) = \mathbf{R}_{z'}\left(\phi'\left(\mathbf{r}, T_\mathrm{R}; \frac{T_\mathrm{P}}{2} + T_\mathrm{E}\right)\right)\mathbf{E}\left(\mathbf{r}, T_\mathrm{R}; \frac{T_\mathrm{P}}{2} + T_\mathrm{E}\right)\mathbf{S}\mathbf{m}'\left(\mathbf{r}, t_0 + \frac{T_\mathrm{P}}{2} + T_\mathrm{E}\right)$$

$$+ \mathbf{m}_0\left(\mathbf{r}, T_\mathrm{R}; \frac{T_\mathrm{P}}{2} + T_\mathrm{E}\right). \tag{2.21}$$

In steady-state, one cycle of excitation, acquisition, spoiling, and recovery returns the magnetization back to its initial state. We enforce this through the steady-state condition

$$\mathbf{m}'(\mathbf{r}, t_0 + T_\mathrm{P}) = \mathbf{R}_{x'}(\alpha(\mathbf{r}, t_0 + T_\mathrm{P}; t_0))\mathbf{m}'(\mathbf{r}, t_0 + T_\mathrm{R}) \tag{2.22}$$

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[2]Transverse signal spoiling is often (nearly) achieved in practice using strong induced field inhomogeneities (which cause rapid transverse signal dephasing) in tandem with RF excitations that additionally impart nonlinear (often quadratically increasing) transverse magnetization phase [14]. Though the nonlinear RF phase used in so-called "RF-spoiling" prevents any one spin from reaching a true steady-state, the signal integrated over a typically-sized voxel achieves SS-like behavior [15].

which yields an algebraic system of equations. When it exists, the solution is

$$\mathbf{m}'(\mathbf{r}, t_0 + T_{\mathrm{P}}) = \frac{1}{1 - e^{-(T_{\mathrm{R}} - T_{\mathrm{P}})/T_1(\mathbf{r})} \cos\left(\alpha(\mathbf{r})\right)} \begin{bmatrix} 0 \\ m_0(\mathbf{r}) \sin\left(\alpha(\mathbf{r})\right)\left(1 - e^{-(T_{\mathrm{R}} - T_{\mathrm{P}})/T_1(\mathbf{r})}\right) \\ m_0(\mathbf{r}) \cos\left(\alpha(\mathbf{r})\right)\left(1 - e^{-(T_{\mathrm{R}} - T_{\mathrm{P}})/T_1(\mathbf{r})}\right) \end{bmatrix},$$

{eq:spgr-bmmp-t0} $\hspace{11cm}$ (2.23)

where $\alpha(\mathbf{r}) := \alpha(\mathbf{r}, t_0 + T_{\mathrm{P}}; t_0)$ is a slight abuse of notation. Remarkably, the SPGR steady-state magnetization immediately after excitation is approximately independent of both off-resonance effects and $T_2(\mathbf{r})$. Researchers more often cite the expression

$$m'_{xy}(\mathbf{r}, t_0 + T_{\mathrm{P}}) = m'_x(\mathbf{r}, t_0 + T_{\mathrm{P}}) + im'_y(\mathbf{r}, t_0 + T_{\mathrm{P}})$$

{eq:spgr-mxyp-t0} $$= \frac{im_0(\mathbf{r}) \sin\left(\alpha(\mathbf{r})\right)\left(1 - e^{-T_{\mathrm{R}}/T_1(\mathbf{r})}\right)}{1 - e^{-T_{\mathrm{R}}/T_1(\mathbf{r})} \cos\left(\alpha(\mathbf{r})\right)} \hspace{2cm} (2.24)$$

for the complex transverse magnetization as it modifies (2.23) to include a simple first-order correction for unaccounted T_1 recovery during the RF pulse. Substituting (2.24) into (2.19) yields an expression for the transverse magnetization at the echo time:

$$m'_{xy}\left(\mathbf{r}, t_0 + \frac{T_{\mathrm{P}}}{2} + T_{\mathrm{E}}\right) = m'_{xy}(\mathbf{r}, t_0 + T_{\mathrm{P}}) e^{-(T_{\mathrm{E}} - T_{\mathrm{P}}/2)/T_2(\mathbf{r})} e^{-i\phi'\left(\mathbf{r}, t_0 + \frac{T_{\mathrm{P}}}{2} + T_{\mathrm{E}}; t_0 + T_{\mathrm{P}}\right)}$$

{eq:spgr-mxyp-te} $$\approx m'_{xy}(\mathbf{r}, t_0 + T_{\mathrm{P}}) e^{-T_{\mathrm{E}}/T_2(\mathbf{r})} e^{-i\phi'\left(\mathbf{r}, t_0 + \frac{T_{\mathrm{P}}}{2} + T_{\mathrm{E}}; t_0 + \frac{T_{\mathrm{P}}}{2}\right)}, \hspace{1cm} (2.25)$$

where the approximation again keeps in line with literature expressions.

The received signal is approximately proportional to the integrated transverse magnetization over a volume $\mathbb{V}$. To derive expressions, we take a few more usual assumptions:

- We assume that the signal is localized to a scale over which there is off-resonance phase variation, but minimal variation of $m_0(\mathbf{r})$, $T_1(\mathbf{r})$, $T_2(\mathbf{r})$, and $\alpha(\mathbf{r})$. This assumption is reasonable[3] when describing the signal arising from a typical voxel.

- We assume that (free-precession) off-resonance phase grows linearly with time, *i.e.* $\phi'\left(\mathbf{r}, t_0 + \frac{T_{\mathrm{P}}}{2} + T_{\mathrm{E}}; t_0 + \frac{T_{\mathrm{P}}}{2}\right) \approx \omega'(\mathbf{r})T_{\mathrm{E}}$. We further assume that off-resonance frequency $\omega'(\mathbf{r})$ is distributed over the localized voxel as $p_{\omega'} \leftarrow \mathrm{Cauchy}(\bar{\omega}', R'_2)$, where $\bar{\omega}'(\mathbf{r})$ is the median off-resonance frequency and $R'_2(\mathbf{r})$ is the broadening bandwidth.

With these additional assumptions, the received steady-state SPGR (noiseless) signal model

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[3]Model mismatch due to within-voxel spatial variation of relaxation parameters can be significant, especially for large voxels. Chapter 6 studies so-called partial volume effects and uses them for QMRI.

for a typically sized voxel centered at position $\mathbf{r}$ is (to within constants):

{eq:spgr-int}
$$s_{\mathrm{S}}\left(\mathbf{r}, t_0 + \frac{T_{\mathrm{P}}}{2} + T_{\mathrm{E}}\right) \propto \int_{\mathbb{V}(\mathbf{r})} m'_{xy}\left(\mathbf{r}, t_0 + \frac{T_{\mathrm{P}}}{2} + T_{\mathrm{E}}\right) \mathrm{d}^3\,\mathbf{r} \tag{2.26}$$

$$\approx m_{xy}(\mathbf{r}, t_0 + T_{\mathrm{P}})e^{-T_{\mathrm{E}}/T_2(\mathbf{r})} \int_{\mathbb{R}} e^{-i\omega' T_{\mathrm{E}}} p_{\omega'}(\omega')\,\mathrm{d}\,\omega'$$

$$= m_{xy}(\mathbf{r}, t_0 + T_{\mathrm{P}})e^{-T_{\mathrm{E}}/T_2(\mathbf{r})}e^{-R_2'(\mathbf{r})T_{\mathrm{E}} - i\bar{\omega}'(\mathbf{r})T_{\mathrm{E}}}$$

{eq:spgr-model}
$$= \frac{im_0(\mathbf{r})\sin\left(\alpha(\mathbf{r})\right)\left(1 - e^{-T_{\mathrm{R}}/T_1(\mathbf{r})}\right)}{1 - e^{-T_{\mathrm{R}}/T_1(\mathbf{r})}\cos\left(\alpha(\mathbf{r})\right)}e^{-T_{\mathrm{E}}/T_2^*(\mathbf{r})}e^{-i\bar{\omega}'(\mathbf{r})T_{\mathrm{E}}}, \tag{2.27}$$

where $T_2^*(\mathbf{r}) := \left(\frac{1}{T_2} + R_2'\right)^{-1}$ is a modified spin-spin relaxation time that accounts for additional transverse magnetization decay due to off-resonance effects.

2.1.2.2 Dual-Echo Steady-State (DESS) Sequence

{sss,bkgrd,mri,ss,dess}

DESS [16, 17] is a fast pulse sequence that interlaces fixed, constant-phase RF excitations with fixed dephasing "gradients" (*i.e.*, induced main field inhomogeneities that vary nearly linearly with space) to produce two distinct signals per RF excitation. Here we develop simple steady-state DESS signal models.

As in Subsection 2.1.2.1, let $\mathbf{m}'(\mathbf{r}, t_0)$ denote the magnetization at an initial time t_0 selected well into the steady-state and just prior to excitation. The DESS sequence first applies a fixed RF rotation $\alpha(\mathbf{r}) := \alpha(\mathbf{r}, t_0 + rT_{\mathrm{R}} + T_{\mathrm{P}}; t_0 + rT_{\mathrm{R}}), \forall r \in \{0, 1, 2, \dots\}$:

{eq:dess-ex}
$$\mathbf{m}'(\mathbf{r}, t_0 + T_{\mathrm{P}}) = \mathbf{R}_{x'}(\alpha(\mathbf{r}))\mathbf{m}'(\mathbf{r}, t_0). \tag{2.28}$$

The excited transverse magnetization contributes to a first acquired signal; dephases (but does not spoil completely) due to gradient dephasing[4] and contributes again to a second (smaller, but nonzero) acquired signal. Since (with proper selection) dephasing gradients mainly contribute to off-resonance phase accrual, the net effect after data acquisition and gradient spoiling is well described simply by precession and relaxation:

{eq:dess-pr}
$$\mathbf{m}'(\mathbf{r}, t_0 + T_{\mathrm{R}}) = \mathbf{R}_{z'}(\phi'(\mathbf{r}))\mathbf{E}(\mathbf{r}, T_{\mathrm{R}}; T_{\mathrm{P}})\mathbf{m}'(\mathbf{r}, t_0 + T_{\mathrm{P}}) + \mathbf{m}_0(\mathbf{r}, T_{\mathrm{R}}; T_{\mathrm{P}}), \tag{2.29}$$

where the abbreviation $\phi'(\mathbf{r}) := \phi'(\mathbf{r}, t_0 + (r+1)T_{\mathrm{R}}; t_0 + rT_{\mathrm{R}} + T_{\mathrm{P}}), \forall r \in \{0, 1, 2, \dots\}$ implies fixed phase accrual (due to gradient dephasing, field inhomogeneity, and other

---

[4]It is worth distinguishing gradient dephasing (commonly but somewhat misleadingly referred to as gradient spoiling) from RF spoiling. Gradient dephasing (used in DESS) primarily affects magnetization phase and is modeled simply as precession. RF spoiling (used in SPGR) combines gradient dephasing with nonlinear RF phase cycling and suppresses magnetization magnitude in steady-state.

unaccounted effects) over each repetition cycle.

In steady-state, one cycle of excitation, first acquisition, gradient spoiling, second acquisition, and (partial) recovery returns the magnetization back to its initial state. We enforce this through the steady-state condition

$$\mathbf{m}'(\mathbf{r}, t_0) = \mathbf{m}'(\mathbf{r}, t_0 + T_{\mathrm{R}}) \tag{2.30}$$

which yields an algebraic system of equations. When it exists, the solution gives the steady-state magnetization just prior to RF excitation:

$$\mathbf{m}'(\mathbf{r}, t_0) = \begin{bmatrix} E_2(\mathbf{r}, T_{\mathrm{F}}) \sin \alpha(\mathbf{r}) \sin \phi'(\mathbf{r}) \\ -E_2(\mathbf{r}, T_{\mathrm{F}}) \sin \alpha(\mathbf{r})(E_2(\mathbf{r}, T_{\mathrm{F}}) - \cos \phi'(\mathbf{r})) \\ 1 - E_2(\mathbf{r}, T_{\mathrm{F}}) \cos \phi'(\mathbf{r}) + E_2(\mathbf{r}, T_{\mathrm{F}}) \cos \alpha(\mathbf{r})(E_2(\mathbf{r}, T_{\mathrm{F}}) - \cos \phi'(\mathbf{r})) \end{bmatrix} q(\mathbf{r}, T_{\mathrm{F}}),$$

$$\tag{2.31}$$

where $T_{\mathrm{F}} := T_{\mathrm{R}} - T_{\mathrm{P}}$ is the free precession interval; $E_1(\mathbf{r}, t) := e^{-t/T_1(\mathbf{r})}$ and $E_2(\mathbf{r}, t) := e^{-t/T_2(\mathbf{r})}$ are relaxation operators; and $q(\mathbf{r}, t) :=$

$$\frac{m_0(\mathbf{r})(1 - E_1(\mathbf{r}, t))}{(1 - E_1(\mathbf{r}, t) \cos \alpha(\mathbf{r}))(1 - E_2(\mathbf{r}, t) \cos \phi'(\mathbf{r})) - E_2(\mathbf{r}, t)(E_1(\mathbf{r}, t) - \cos \alpha(\mathbf{r}))(E_2(\mathbf{r}, t) - \cos \phi'(\mathbf{r}))}.$$

Substituting (2.31) into (2.28) produces a similar expression for the steady-state magnetization immediately following RF excitation:

$$\mathbf{m}'(\mathbf{r}, t_0 + T_{\mathrm{P}}) = \begin{bmatrix} E_2(\mathbf{r}, T_{\mathrm{F}}) \sin \alpha(\mathbf{r}) \sin \phi'(\mathbf{r}) \\ \sin \alpha(\mathbf{r})(1 - E_2(\mathbf{r}, T_{\mathrm{F}}) \cos \phi'(\mathbf{r})) \\ \cos \alpha(\mathbf{r})(1 - E_2(\mathbf{r}, T_{\mathrm{F}}) \cos \phi'(\mathbf{r})) + E_2(\mathbf{r}, T_{\mathrm{F}})(E_2(\mathbf{r}, T_{\mathrm{F}}) - \cos \phi'(\mathbf{r})) \end{bmatrix} q(\mathbf{r}, T_{\mathrm{F}}).$$

$$\tag{2.32}$$

The transverse magnetizations before and after RF excitation are then

$$m'_{xy}(\mathbf{r}, t_0) = -i \sin \alpha(\mathbf{r}) E_2(\mathbf{r}, T_{\mathrm{R}}) \Big(E_2(\mathbf{r}, T_{\mathrm{R}}) - e^{-i\phi'(\mathbf{r})} \Big) q(\mathbf{r}, T_{\mathrm{R}}); \tag{2.33}$$

$$m'_{xy}(\mathbf{r}, t_0 + T_{\mathrm{P}}) = +i \sin \alpha(\mathbf{r}) \Big(1 - E_2(\mathbf{r}, T_{\mathrm{R}}) e^{i\phi'(\mathbf{r})} \Big) q(\mathbf{r}, T_{\mathrm{R}}), \tag{2.34}$$

where (2.33)-(2.34) include simple first-order corrections for yet-unaccounted relaxation and recovery during excitation. Frequently, the DESS signals are acquired at symmetric echo times T_{E} before and after the center of each RF pulse. Substituting (2.34) into (2.9)

gives the magnetization at the data acquisition time after RF excitation:

$$m'_{xy}\left(\mathbf{r}, t_0 + \frac{T_\mathrm{P}}{2} + T_\mathrm{E}\right) = m'_{xy}(\mathbf{r}, t_0 + T_\mathrm{P})e^{-(T_\mathrm{E}-T_\mathrm{P}/2)/T_2(\mathbf{r})}e^{-i\phi'\left(\mathbf{r},t_0+\frac{T_\mathrm{P}}{2}+T_\mathrm{E};t_0+T_\mathrm{P}\right)}$$

$$\approx m'_{xy}(\mathbf{r}, t_0 + T_\mathrm{P})e^{-T_\mathrm{E}/T_2(\mathbf{r})}e^{-i\phi'\left(\mathbf{r},t_0+\frac{T_\mathrm{P}}{2}+T_\mathrm{E};t_0+\frac{T_\mathrm{P}}{2}\right)} \qquad (2.35)$$

$$\approx m'_{xy}(\mathbf{r}, t_0 + T_\mathrm{P})e^{-T_\mathrm{E}/T_2(\mathbf{r})}e^{-i\omega'(\mathbf{r})T_\mathrm{E}}, \qquad (2.36)$$

where in (2.35) we again approximately correct for relaxation during excitation and in (2.36) we assume linear off-resonance phase accrual during free precession. To compute the magnetization at the acquisition time before excitation, we consider the free precession and relaxation that occurs between[5] signal reception and excitation:

$$m'_{xy}(\mathbf{r}, t_0) = m'_{xy}\left(\mathbf{r}, t_0 - \left(T_\mathrm{E} - \frac{T_\mathrm{P}}{2}\right)\right)e^{-(T_\mathrm{E}-T_\mathrm{P}/2)/T_2(\mathbf{r})}e^{-i\phi'\left(\mathbf{r},t_0;t_0-\left(T_\mathrm{E}-\frac{T_\mathrm{P}}{2}\right)\right)}. \qquad (2.37)$$

Rearranging (2.37) and applying approximations similar to those of (2.35)-(2.36),

$$m'_{xy}\left(\mathbf{r}, t_0 + \frac{T_\mathrm{P}}{2} - T_\mathrm{E}\right) = m'_{xy}(\mathbf{r}, t_0)e^{+(T_\mathrm{E}-T_\mathrm{P}/2)/T_2(\mathbf{r})}e^{+i\phi'\left(\mathbf{r},t_0;t_0-\left(T_\mathrm{E}-\frac{T_\mathrm{P}}{2}\right)\right)}$$

$$\approx m'_{xy}(\mathbf{r}, t_0)e^{+T_\mathrm{E}/T_2(\mathbf{r})}e^{+i\phi'\left(\mathbf{r},t_0+\frac{T_\mathrm{P}}{2};t_0+\frac{T_\mathrm{P}}{2}-T_\mathrm{E}\right)} \qquad (2.38)$$

$$\approx m'_{xy}(\mathbf{r}, t_0)e^{+T_\mathrm{E}/T_2(\mathbf{r})}e^{+i\omega'(\mathbf{r})T_\mathrm{E}}. \qquad (2.39)$$

The received signal is approximately proportional to the integrated transverse magnetization over a volume $\mathbb{V}$. To derive expressions, we retake assumptions used in Subsection 2.1.2.1 and append an additional assumption on the full-repetition phase accrual $\phi'(\mathbf{r})$:

- We assume that the signal is localized to a scale over which there is off-resonance phase variation, but minimal variation of $m_0(\mathbf{r})$, $T_1(\mathbf{r})$, $T_2(\mathbf{r})$, and $\alpha(\mathbf{r})$. This assumption is reasonable[6] when describing the signal arising from a typical voxel.

- We assume that free precession off resonance frequency $\omega'(\mathbf{r})$ is distributed over the localized voxel as $p_{\omega'} \leftarrow \mathrm{Cauchy}(\bar{\omega}', R'_2)$, where $\bar{\omega}'(\mathbf{r})$ is the median off-resonance frequency and $R'_2(\mathbf{r})$ is the broadening bandwidth.

- We assume that the dephasing gradient imparts an integral number n_cyc of across-

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[5]Observe that we do not attempt to express the magnetization prior to (the next) RF excitation by simply operating on the magnetization after (the current) RF excitation with further precession and relaxation. The reason is due to the intermediate dephasing gradient, which causes phase accrual in excess of off-resonance effects and thus forbids an approximation akin to (2.36).

[6]Model mismatch due to within-voxel spatial variation of relaxation parameters can be significant, especially for large voxels. Chapter 6 studies so-called partial volume effects and uses them for QMRI.

voxel phase cycles[7] such that full-repetition phase accrual $\phi'(\mathbf{r})$ is distributed essentially uniformly as $p_{\phi'} \leftarrow \text{uniform}(0, 2\pi n_{\text{cyc}}), n_{\text{cyc}} \in \{1, 2, 3, \ldots\}$.

With these assumptions, the received steady-state DESS (noiseless) signal models for a typically sized voxel centered at position $\mathbf{r}$ are (to within constants):

{eq:dess-def-int}
$$s_{\text{D}}\left(\mathbf{r}, t_0 + \frac{T_{\text{P}}}{2} + T_{\text{E}}\right) \propto \int_{\mathbb{V}(\mathbf{r})} m'_{xy}\left(\mathbf{r}, t_0 + \frac{T_{\text{P}}}{2} + T_{\text{E}}\right) \text{d}^3\,\mathbf{r} \tag{2.40}$$

$$\approx \int_{\mathbb{R}} \int_{\mathbb{R}} m'_{xy}\left(\mathbf{r}, t_0 + \frac{T_{\text{P}}}{2} + T_{\text{E}}\right) p_{\phi'}(\phi') p_{\omega'}(\omega')\,\text{d}\,\phi'\,\text{d}\,\omega'$$

$$\approx e^{-T_{\text{E}}/T_2(\mathbf{r})} \int_{\mathbb{R}} m'_{xy}(\mathbf{r}, t_0 + T_{\text{P}}) p_{\phi'}(\phi')\,\text{d}\,\phi' \int_{\mathbb{R}} e^{-i\omega' T_{\text{E}}} p_{\omega'}(\omega')\,\text{d}\,\omega'$$

$$= +i m_0(\mathbf{r}) E_2(\mathbf{r}, T_{\text{E}}) e^{-\left(R'_2(\mathbf{r}) - i\bar{\omega}'(\mathbf{r})\right) T_{\text{E}}} \tan\frac{\alpha(\mathbf{r})}{2}\left[1 - \frac{\eta(\mathbf{r}, T_{\text{R}})}{\xi(\mathbf{r}, T_{\text{R}})}\right];$$

{eq:dess-def-model}
$$\tag{2.41}$$

{eq:dess-ref-int}
$$s_{\text{D}}\left(\mathbf{r}, t_0 + \frac{T_{\text{P}}}{2} - T_{\text{E}}\right) \propto \int_{\mathbb{V}(\mathbf{r})} m'_{xy}\left(\mathbf{r}, t_0 + \frac{T_{\text{P}}}{2} - T_{\text{E}}\right) \text{d}^3\,\mathbf{r} \tag{2.42}$$

$$\approx \int_{\mathbb{R}} \int_{\mathbb{R}} m'_{xy}\left(\mathbf{r}, t_0 + \frac{T_{\text{P}}}{2} - T_{\text{E}}\right) p_{\phi'}(\phi') p_{\omega'}(\omega')\,\text{d}\,\phi'\,\text{d}\,\omega'$$

$$\approx e^{+T_{\text{E}}/T_2(\mathbf{r})} \int_{\mathbb{R}} m'_{xy}(\mathbf{r}, t_0) p_{\phi'}(\phi')\,\text{d}\,\phi' \int_{\mathbb{R}} e^{+i\omega' T_{\text{E}}} p_{\omega'}(\omega')\,\text{d}\,\omega'$$

$$= -i m_0(\mathbf{r}) E_2^{-1}(\mathbf{r}, T_{\text{E}}) e^{-\left(R'_2(\mathbf{r}) + i\bar{\omega}'(\mathbf{r})\right) T_{\text{E}}} \tan\frac{\alpha(\mathbf{r})}{2}[1 - \eta(\mathbf{r}, T_{\text{R}})],$$

{eq:dess-ref-model}
$$\tag{2.43}$$

where (2.41) and (2.43) introduce intermediate variables

$$\eta(\mathbf{r}, t) := \sqrt{\frac{1 - E_2^2(\mathbf{r}, t)}{1 - E_2^2(\mathbf{r}, t)/\xi^2(\mathbf{r}, t)}};$$

$$\xi(\mathbf{r}, t) := \frac{1 - E_1(\mathbf{r}, t)\cos\alpha(\mathbf{r})}{E_1(\mathbf{r}, t) - \cos\alpha(\mathbf{r})}.$$

In steady-state, the DESS signal is typically greatest immediately following excitation and defocuses with rate $\frac{1}{T_2} + R'_2$ until what we hereafter denote the *defocusing* echo time.

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[7]In theory, it suffices to design dephasing gradients to impart as few as one complete cycle of net phase variation across a voxel. In practice, field inhomogeneities will induce spurious through-voxel field gradients that modify the effective dephasing gradient moment and thereby create partial phase cycles that distort the nominally uniform phase distribution. To reduce model mismatch due to such "partial spoiling" effects, dephasing gradients are usually designed to nominally impart multiple complete cycles of across-voxel phase variation. However, larger dephasing gradients cause greater DESS model mismatch due to diffusive signal loss. Appendix B studies diffusion in DESS and discusses regimes of dephasing gradient moments which balance partial-spoiling versus diffusive sources of model mismatch.

After a low-signal period between RF pulses, the DESS signal then refocuses with rate $\frac{1}{T_2} - R_2'$ from what we hereafter denote the *refocusing* echo time until just prior the next excitation. Fortuitously, the defocusing (2.41) and refocusing (2.43) DESS signal models have significantly different dependence on relaxation parameters (especially T_2) and thus together are quite useful for relaxation parameter estimation.

2.2   Optimization in QMRI

This section overviews how optimization methods are leveraged in a substantial portion of this thesis to solve practical QMRI problems. For such problems, the central idea is to construct a suitable scalar cost function Ψ of some design variables $\mathbf{x}$, whose output $\Psi(\mathbf{x}) \in \mathbb{R}$ is designed to provide a measure of the undesirability of $\mathbf{x}$. We then employ tailored optimization algorithms to find an $\mathbf{x}$ that minimizes Ψ over a set $\mathbb{X}$, written as

$$\mathbf{x}^* \in \left\{ \arg \min_{\mathbf{x} \in \mathbb{X}} \Psi(\mathbf{x}) \right\}. \tag{2.44}$$

In either optimization-based parameter estimation (Chapter 3) or acquisition design (Chapter 4), we have reason to design Ψ to depend on corresponding design variables $\mathbf{x}$ through MR signal models. Because these models are often (strongly) nonlinear functions of design variables, corresponding cost functions are usually non-convex in $\mathbf{x}$ (though the search space $\mathbb{X}$ is almost always assumed convex in this thesis). Thus, most QMRI problems in the form of (2.44) are non-convex optimization problems.

In general, solving (2.44) is more challenging when Ψ is non-convex in $\mathbf{x}$ than otherwise, due in part to the possible presence of local extrema and/or saddle points. In the following, we discuss two strategies used in this thesis to cope with non-convex optimization. Subsection 2.2.1 relaxes (2.44) to seek a local (instead of global) minimizer via iterative methods. Subsection 2.2.2 restricts attention to signal models that are linear in a portion of $\mathbf{x}$ and discusses a simplification of (2.44) for such partially linear structures.

2.2.1   Iterative Local Optimization with Constraints

This subsection overviews a method for finding a local minimizer $\widehat{\mathbf{x}}$ of possibly non-convex cost function Ψ over convex constraint set $\mathbb{X}$. Such $\widehat{\mathbf{x}} \in \mathbb{X}$ must satisfy for some $\delta > 0$

$$\Psi(\widehat{\mathbf{x}}) \leq \Psi(\mathbf{x}) \qquad \forall \mathbf{x} \in \mathbb{X} : \|\widehat{\mathbf{x}} - \mathbf{x}\|_2 < \delta. \tag{2.45}$$

Observe that a global optimizer $\mathbf{x}^*$ satisfies (2.45) for arbitrarily large δ; thus, any global minimizer is a local minimizer (but the converse is not necessarily true unless Ψ is convex).

As even locally optimal minimizers are often challenging to compute analytically, many algorithms construct $\widehat{\mathbf{x}}$ by iteratively updating an initial guess $\mathbf{x}^{(0)}$ until some convergence criterion is satisfied. For a differentiable cost and convex constraints, the gradient projection method [18] is one such iterative algorithm and repeats the following simple update:

$$\mathbf{x}^{(i)} \leftarrow P_{\mathbb{X}}\big(\mathbf{x}^{(i-1)} - \mathbf{\Pi}\nabla_{\mathbf{x}}\Psi\big(\mathbf{x}^{(i-1)}\big)\big), \tag{2.46}$$

where $P_{\mathbb{X}}$ denotes projection onto $\mathbb{X}$ and $\mathbf{\Pi}$ is a diagonal preconditioning matrix that permits elements of $\mathbf{x}$ to take scale-informed step sizes along the negative gradient direction.

If Ψ is convex and sufficiently smooth, iterates produced via (2.46) converge to a limit point [19] that is a constrained global minimum (for appropriately selected $\mathbf{\Pi}$). If instead Ψ is non-convex (but $\mathbb{X}$ is still convex), statements regarding convergence[8] to a particular constrained local minimizer require additional (strong) assumptions regarding initialization and in general are still much weaker than in the convex case.

Since non-convex cost functions can have many local extrema (whose associated costs can vary dramatically), the utility of a locally optimal solution depends strongly on initialization quality. Accordingly, this thesis uses iterative local optimization for non-convex QMRI problems where a reasonable initialization is available and global optimization (to within quantization error) via exhaustive grid search is intractable.

2.2.2 Partially Linear Models and the Variable Projection Method

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[8]For example, it suffices to assume that $\mathbf{x}^{(0)}$ lies in the *attraction basin* $\mathbb{B}_{\tilde{\mathbf{x}}}$ of a given unconstrained local minimum $\tilde{\mathbf{x}}$, where attraction basin is defined here as the largest convex set containing $\tilde{\mathbf{x}}$ over which Ψ is convex. If $\mathbb{B}_{\tilde{\mathbf{x}}} \cap \mathbb{X}$ is nonempty and step sizes within $\mathbf{\Pi}$ are small enough to contain iterates within $\mathbb{B}_{\tilde{\mathbf{x}}}$, then iterates converge to the limit point $P_{\mathbb{X}}(\tilde{\mathbf{x}})$.

CHAPTER 3

MRI Parameter Estimation
from Likelihood Models

{c,relax}

CHAPTER 4

Optimizing MR Scan Design
for Model-Based Relaxometry

{c,scn-dsgn}

CHAPTER 5

MRI Parameter Estimation
via Kernel Regression

{c,krr}

CHAPTER 6

Myelin Water Fraction Estimation from Steady-State Sequences

{c,mwf}

CHAPTER 7

Steady-State RF Pulse Design

{c,ss-rf}

CHAPTER 8

Future Work

{c,future}

APPENDIX A

Coil Data Combination from Multiple Datasets

{a,cc-multi}

APPENDIX B

DESS in the Presence of Diffusion

{a,dess-diff}

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