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B1 Mapping for Magnetic Resonance Imaging

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$B_1$ Mapping for Magnetic Resonance Imaging

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A dissertation submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

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Magnetic Resonance Imaging (MRI) is a non-ionizing form of medical imaging which has practical uses in diagnosing, characterizing, and studying diseases in vivo. Current clinical practice utilizes a highly trained radiologist to view MR images and qualitatively diagnose, characterize, or study a disease. There is no easy way to compare qualitative data. That is why developing quantitative measures in MRI show promise. Quantitative measures of disease can be compared across a population, MRI sites, and over time. Osteoarthritis is one disease where those who have it may benefit from the development of quantitative MRI measures. Those benefits may include earlier diagnosis and treatment of the disease or treatment which may halt or even reverse the damage from the disease.

The work presented in this dissertation focuses on analyzing and developing new methods of radiofrequency ($B_1$) field mapping to improve quantitative MRI measures. The dissertation opens with an introduction and a brief primer on MRI physics, followed by an introduction to $B_1$ and flip-angle mapping in MRI (Chapters 1–3). Chapter 4 presents a careful statistical analysis of a recent and popular $B_1$ mapping method, the Bloch-Siegert shift (BSS) method, along with a comparison of the technique to other common $B_1$ mapping methods. The statistical models developed in chapter 4 are verified using both Monte Carlo simulation and actual MRI experiments in phantoms. Chapter 5 analyzes and details the potential errors introduced in $B_1$ mapping when a 3D slab-selective excitation is employed. A method for correcting errors introduced by 3D slab-selective $B_1$ mapping is then introduced in chapter 6, along with metrics to quantify the error involved. The thesis closes with a summary of other scientific contributions made by the author in chapter 7. The chapters comprising the bulk of the presented research (4-7) are briefly summarized below.

Chapter 4, the statistical analysis of $B_1$ mapping methods, demonstrates the effectiveness of deriving the $B_1$ estimate from the phase of the MR image. These techniques are shown to perform particularly well in low signal-to-noise ratio (SNR) applications. However, there are benefits and drawbacks of each $B_1$ mapping technique. The BSS method deposits a significant amount of radiofrequency (RF) power into the patient, causing a concern that tissue heating may occur. The Phase-Sensitive (PS) method of $B_1$ mapping outperforms the other techniques in many situations, but suffers from significant sensitivity to off-resonance. The Dual-Angle (DA) method is very simple to implement and the analysis is straightforward, but it can introduce significant mean bias in the estimate. No $B_1$ mapping technique performs well for all situations. Therefore, the best $B_1$ mapping method needs to be determined for each situation. The work in chapter 4 provides guidance for that choice.
Many $B_1$ mapping techniques rely on a linear relationship between flip angle and transmit voltage. That assumption breaks down when a 3D slab-selective excitation is used. 3D slab-selective excitation is a common technique used to reduce the field-of-view (FOV) in MRI, which can directly reduce scan time. The problem with slab-selective excitation in conjunction with $B_1$ mapping has been documented, but the potential errors in $B_1$ estimation have never been properly analyzed across different techniques. The analysis in chapter 5 demonstrates that the errors introduced in $B_1$ mapping using a slab-selective excitation in conjunction with the ubiquitous DA $B_1$ mapping method can be significant. It is then shown that another $B_1$ mapping technique, the Actual Flip Angle Imaging (AFI) method, doesn’t suffer from the same limitation.

The analysis presented in Chapter 6 demonstrates that some errors introduced by 3D slab-selective $B_1$ mapping may be modeled and corrected allowing the use of 3D slab-selective excitation to reduce field-of-view, and potentially reduce scan time. The errors are modeled and corrected with a general numerical method using Bloch simulations. The general method is applied to the DA method as an example, but is general and could easily be extended to other methods as well. Finally, a set of metrics are proposed and briefly explored that can be used to better understand the topology and severity of errors introduced into $B_1$ mapping methods. With a better understanding of the errors introduced, the need for correction can be determined.

Chapter 7 details other significant ancillary contributions made by the author including: (1) presentation of a new $B_1$ mapping method, the decoupled RF-pulse phase-sensitive $B_1$ mapping method, which has potential for parallel transmit MRI; (2) demonstration of an ultra-short TE method which has potential for imaging Alzheimers brain lesions \textit{in vivo}; (3) introduction of a new steady-state diffusion tensor imaging technique; (4) phase-sensitive $B_1$ mapping in sodium is demonstrated, a feat not previously demonstrated; (5) a comparison between a dual-tuned and single-tuned sodium coil; (6) introduction of a water- and fat-separation technique using multiple acquisition SSFP; (7) an inter-site and inter-vendor quantitative MRI study is introduced; (8) a relaxation and contrast optimization for laryngeal imaging at 3T is introduced; and (9) diffusion imaging with insert gradients is introduced.

Keywords: magnetic resonance imaging, flip-angle mapping, $B_1$ mapping, Bloch-Siegert shift, phase sensitive, dual angle, actual flip angle imaging, BSS, PS, DA, AFI, slab selection, 3D, slice selection, flip angle, $B_1$
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Chapter 1

Introduction

Magnetic Resonance Imaging (MRI) is a non-ionizing form of medical imaging used to non-invasively visualize the structure and function of living tissues. The first two-dimensional (2D) image was published by Paul Lauterbur in 1973[1] based on an idea he introduced the prior year [2]. Sir Peter Mansfield introduced faster imaging techniques starting in 1976 [3, 4]. Since that time, the field of MRI has exploded. It is used for methods varying from metabolic imaging to real time cardiac imaging and from functional MRI (fMRI) of the brain and other parts of the body to diffusion imaging of all parts of the body. MRI is an invaluable diagnostic tool which is continuing to improve and demonstrate new benefits to understanding the human body, diagnosing and characterizing disease, and developing new treatments.

1.1 Motivation

Current clinical MRI techniques depend on a highly trained radiologist determining abnormalities by looking at the MRI images. The assessment is almost always qualitative. A few examples include: a tear might be identified in the ACL or meniscus in the knee joint simply due to the presence of a bright signal from synovial fluid where there should be uninterrupted dark signal from the ligament or meniscus; a herniation of one of the intervertebral discs might be identified by a mass bulging out of the disc and slightly displacing the spinal cord; or the presence of a tumor or cyst might be identified. These qualitative assessments are invaluable but are difficult to compare and track over time.

While quantitative morphological measurements are often performed (i.e., measurements of the dimensions of anatomical features identified in the image), quantitative analysis of many other physiological parameters that could be studied with MRI are difficult and not
in common clinical usage. However, such quantitative analyses of other physiological parameters could have a profound impact on the discovery and evaluation of new drugs and treatments, diagnostic accuracy, and the evaluation of ongoing treatment efficacy.

Development of quantitative measurements is a new and exciting field. Many routes are being explored to find these quantitative metrics. However, a confounding factor for finding and developing these metrics is varying signal intensity across a single tissue. Uncorrected variation in signal intensity leads to a variation in quantitative metrics. The cause of signal intensity variation across a single tissue is variation in the radio frequency (RF or $B_1$) field used for imaging. Therefore, almost all of the truly quantitative measures that one might wish to perform using MRI would rely necessarily on an accurate assessment of the radio frequency (or $B_1$) fields present during imaging. Thus, $B_1$ mapping is an extremely important and active area of research.

The specific work in this dissertation was motivated by the need for accurate $B_1$ maps for the development of quantitative measures for the study of osteoarthritis (OA). OA outcomes have the potential to significantly improve if the progression of the disease could be assessed through non-invasive imaging at a very early stage. As of this writing, assessment of the progression of osteoarthritis is usually done by measuring the thickness and/or volume of the cartilage from the MRI image. These changes in cartilage thickness and volume are only evident at a very late stage of disease progression. Once cartilage degeneration begins to appear on conventional MRI images, it is typically too late to treat [5, 6]. However, very early biochemical changes in cartilage that portend the onset of OA have been shown to be potentially reversible. A non-invasive tool is needed to test potential treatments at this early stage.

This is where quantitative MRI shows promise. One class of molecules in cartilage called proteoglycans begin to deplete in the early stages of osteoarthritis before cartilage volume loss occurs. Proteoglycans have a negative charge which is directly offset with positively charged sodium ions. As the proteoglycans deplete, the sodium concentration also decreases. This is significant because sodium nuclei are MR visible. If the sodium concentration in cartilage can be quantified in an MR image, a decrease in sodium concentration may be an early indicator of osteoarthritis. Thus, the result of being able to identify the decrease in sodium
concentration could result in drugs or treatments that halt and/or reverse the progression of OA. In other words, cartilage degeneration and the resultant suffering could be a thing of the past. With current late stage measurements of cartilage thickness, the development of drugs and/or treatments for OA require years to complete and incur significant cost.

However, MR sodium images depend on more than just the sodium concentration. The images also depend on factors such as radio frequency field intensity and intrinsic MR parameters, $T_1$ and $T_2$. As the MR physics lab at Brigham Young University pushed the development of quantitative sodium MRI for the assessment of early degeneration in cartilage forward, it became abundantly evident that there was a need to produce good 3D sodium $B_1$ maps in the inherently very low SNR environment of sodium MRI. This research and dissertation has focused on improving the knowledge of the radio frequency (RF) field distribution, which has proved to be a huge undertaking in and of itself.

In addition to the work on sodium MRI that motivated my exploration of $B_1$ mapping, the topic has become increasingly important in the broader MR community with the advent of higher field MRI systems (such as the 7 Tesla systems that are being installed at research institutions around the world). High-field MRI systems deposit significantly more RF power in patients (due to the higher Larmor frequency, as described in chapter 2). As a consequence, understanding and mapping the $B_1$ fields is of the utmost importance for patient safety.

While my contributions that are discussed throughout the remainder of this dissertation were motivated by some of the quantitative MRI techniques (primarily quantitative sodium MRI and quantitative high-field MRI) discussed, it is very important to note that my contributions and the bulk of my time as a graduate student have been spent very specifically focusing on some fundamental problems associated with $B_1$ mapping, and analysis of $B_1$ mapping techniques in common usage. The analyses and work presented are directly applicable to hundreds of diverse applications in MRI (quantitative and otherwise), particularly as high field (7T and above) scanners become commonplace in the research community. While my contributions may seem highly specialized and focused to the reader not actively involved in MRI research, the problems associated with rapid, accurate $B_1$ assessment are one of the major areas of focus currently in MRI research, and are extremely topical. The analyses, techniques, and metrics proposed herein can be directly applied to a vast array of
research topics; therefore, the decision was made to present them for the most part without reference to specific applications.

1.2 Previous Work

Magnetic resonance imaging (MRI) would not have been possible without Felix Bloch and Edward Purcell independently publishing their work on Nuclear Magnetic Resonance (NMR) induction in 1946[7, 8, 9, 10]. Although not well known, the first one-dimensional MR image was demonstrated by Herman Carr and described in his 1953 Harvard doctoral thesis[11]. As previously mentioned, Paul Lauterbur and Sir Peter Mansfield have been credited with the first two-dimensional (2D) MR image and for introducing an imaging technique that notably accelerates image acquisition, respectively. For their contributions, they were jointly awarded the Nobel Prize in Physiology or Medicine in 2003.

In Lauterbur’s 1973 article in Nature [1], he states that the “signal in the presence of a [magnetic] field gradient represents a one-dimensional projection of the $H_2O$ content of the object” when “assuming uniform signal strength across the region within the transmitter-receiver coil.” (emphasis added) This statement by Lauterbur implies the importance of knowing the field from the transmitter-receiver coil if it is not uniform.

The transmitter-receiver RF field is often called the $B_1$ field in MRI. Mapping the relative or absolute values of this field is called $B_1$ mapping. The goal of $B_1$ mapping is usually to determine how an MRI parameter known as the “flip angle” (to be described in chapter 2) varies spatially across an image in two or three dimensions. For this reason, the flip angle is often calculated directly without an intermediate estimate of the $B_1$ field being computed. Although there are subtle differences between flip angle mapping and $B_1$ mapping, these will sometimes be referred to interchangeably. The focus of this thesis is $B_1$ mapping.

The first precursors to $B_1$ maps in MRI were provided in 1986 when McVeigh et al. [12] calculated the sensitivity of a receive coil, and corroborated his findings using images of a uniform phantom. This data was used to correct non-uniformities in the image intensity. Axel et al. [13] also described a method to correct image intensity variations when imaging with a surface coil with a severely non-uniform field distribution. Intensity
Correction in images is an important use of $B_1$ mapping. However, it is still typically used to improve qualitative assessments of an image, rather than to enable true quantitation of some physiological parameter.

$B_1$ maps that aided quantitation began in 1987 when Murphy-Boesch et al. [14] introduced a two dimensional (2D) method of quantitatively measuring the $B_1$ field by measurement of the “flip angle”. Another quantitative $B_1$ mapping technique was introduced by Oh et al. [15] in 1990 which will be referred to as the Spin Echo Phase-Sensitive (SEPS) method. That technique uses a special RF pulse after excitation to encode the flip angle achieved into the phase of the resulting image. Flip angle and $B_1$ strength are directly related in most cases. Other major $B_1$ mapping methods introduced include the Dual-Angle (DA) method [16], the Actual Flip-angle Imaging (AFI) method [17], the Phase-Sensitive (PS) method [18], and the Bloch-Siegert Shift (BSS) method [19].

Methods of $B_1$ mapping that rely on changing $B_1$ field strength are implicitly assuming that $B_1$ field strength scales uniformly across a volume. However, this assumption is violated when selective excitation pulses are used to produce both 2D images and field-of-view limited three-dimensional (3D) images, a common method to reduce scan time. It is well known that a selective excitation pulse introduces errors into $B_1$ mapping as documented by Bouhrara and Bonny [20] in 2012. Their analysis focuses on the effects of slice selection to produce 2D images on $B_1$ mapping and ways to correct for these effects. However, no similar analysis exists that expands this to 3D. While the extension to 3D shares some common elements with the 2D treatment, there are some very important and subtle differences. Not all slices in a volume excited with 3D slab selection will have significant error. The analysis in chapters 5 and 6 shed light on that effect, and present a method for correcting those errors.

1.3 Contributions

There are three major ways and some ancillary ways I have contributed while at Brigham Young University. The first major way included developing a statistical model of the Bloch-Siegert Shift (BSS) $B_1$ mapping method for MRI, performing a careful comparison of this technique with several other popular $B_1$ mapping techniques, and validating the model.
through both Monte Carlo simulation and experiment (see chapter 4 and [21, 22, 23]). The second major way included performing a careful evaluation of the limitations of $B_1$ mapping in the presence of a 3D slab-selective gradient (see chapter 5). The third major way includes proposing and developing a general numerical method for correcting errors in $B_1$ mapping introduced by 3D slab-selective gradients along with metrics for assessing the errors (and improvements through correction) in the $B_1$ maps (see chapter 6). Likewise, chapter 7 presents some of my important ancillary contributions including a new $B_1$ mapping technique based on the phase-sensitive method that may have application to parallel-transmit MRI [24], the development and analysis of a phase-sensitive $B_1$ mapping technique for sodium MRI [25], the development of MRI pulse sequences for sodium MRI, a new fat/water separation technique in MRI [26], the development of a 3D ultra-short echo time (UTE) pulse sequence using a 3D cones trajectory [27], and the design and construction of a parallel transmit array for the new 7T scanner at the University of Oxford to name just a few.

The paper, “A Statistical Analysis of the Bloch-Siegert $B_1$ Mapping Technique” [23], and chapter 4 offer a statistical analysis of the BSS method along with empirical verification of the statistical model used by Morrell and Schabel [28]. My personal contributions include (1) the idea to analyze the BSS method, (2) the unique analysis due to the method leveraging the Bloch-Siegert shift (a technique that is not typically used in MR imaging), and (3) the experiment design for the empirical verification of the model.

Chapter 5 discusses errors in 3D selective $B_1$ mapping. I identified the cause of errors in $B_1$ mapping due to a 3D slab selective gradient during imaging while helping a fellow student, Haonan Wang, with his project. This effect is demonstrated with Bloch simulations and an experiment designed to validate the simulation results.

Because the simulations can be used for accurately predicting the error introduced by $B_1$ mapping in the presence of 3D slab-selective gradients, the results of those simulations can be used to correct errors (see chapter 6). I defined metrics for these errors so that quantitative improvements may be shown. This method is general because any $B_1$ mapping method can be represented in a Bloch simulation. The results of the Bloch simulation may be used to generate a look-up-table to estimate the $B_1$ field strength or flip angle.

6
Finally, chapter 7 details many of the projects I have assisted with along with my contribution to each project.

1.4 Outline

This dissertation is organized as follows:

1.4.1 MRI Physics Primer

Chapter 2 introduces the basic concepts in Magnetic Resonance Imaging that are used in later chapters.

1.4.2 $B_1$ Mapping Introduction Primer

Chapter 3 introduces the concept of $B_1$ mapping and some descriptions of different methods of $B_1$ mapping to lay a foundation for the presentation of work in later chapters.

1.4.3 Bloch-Siegert Shift Statistical Analysis

Chapter 4 is an analysis of a newly presented $B_1$ mapping method, the Bloch-Siegert Shift (BSS) $B_1$ mapping method. This chapter expands the technique of Morrell to include the BSS method. Furthermore, the experimental verification of the theory presented by Morrell is provided. The phase-based methods analyzed, Bloch-Siegert shift and phase-sensitive methods, display superior performance in low SNR environments with the phase-sensitive method out performing the other analyzed methods in terms of lowest standard deviation and lowest mean bias.

1.4.4 $B_1$ Mapping Errors in the Presence of 3D Slab-Selective Gradients

Chapter 5 introduces the effect of 3D slab-selective excitation on $B_1$ mapping. 3D slab-selective $B_1$ mapping is a technique to limit the scan time by narrowing the field of view with a pulse that only excites one section of the volume to be imaged. This decreases scan time because less of the volume needs to be imaged. It is common in practice. However, there is no discussion in the literature of how the presence of a 3D slab-selective excitation affects $B_1$ mapping methods. This chapter is an introduction to this particular effect. Above all, the
effect is shown to potentially introduce significant errors into $B_1$ mapping. The trend in MR imaging is to reduce scan time which typically means shorter RF pulses. As a consequence, the errors tend to get worse as the RF pulse length shortens.

1.4.5 Correction of $B_1$ Mapping in the Presence of 3D Slab-Selection

Chapter 6 builds on chapter 5 by introducing a method for correcting the errors introduced by using a 3D slab-selective excitation with $B_1$ mapping along with metrics to measure the error. The correction method is applied to the commonly used DA method of $B_1$ mapping. However, the error correction method is general and may be applied to any $B_1$ mapping method that can be represented with a Bloch simulation. Correction of the errors in 3D slab-selective excitation $B_1$ mapping will allow use of common $B_1$ mapping methods that would not have acceptable performance otherwise.

1.4.6 Other Contributions

Chapter 7 outlines some other significant ancillary contributions of the author:

- A $B_1$ mapping method is introduced, the decoupled RF-pulse phase-sensitive $B_1$ mapping method, which has potential for $B_1$ mapping in parallel transmit MRI [24]. High-field MRI suffers from inhomogeneous $B_1$ fields and high specific absorption rates (SAR). Parallel transmit MRI has the potential to mitigate both these problems. However, it requires good $B_1$ maps of all coils involved. The constraints of parallel transmit MRI render many $B_1$ mapping methods impractical. This method is one of few that may be practical in parallel transmit MRI where no method has shown to be the ideal solution.

- An ultra-short TE method is discussed which has potential for imaging Alzheimer’s brain lesions in vivo [27]. This study is very preliminary in an ex vivo brain sample with known Alzheimer’s. If this technique could be used to identify Alzheimer’s brain lesions in vivo, more direct studies of the causes and effects of the disease would be enabled. These direct studies would lead to better outcomes for those who contract Alzheimer’s.
• A new steady-state diffusion tensor imaging technique is introduced. Currently diffusion imaging suffers from long scan times and image warping because of the fast imaging techniques used. This technique could reduce image warping and reduce scan time for diffusion imaging.

• Phase-sensitive $B_1$ mapping in sodium is demonstrated, a feat not previously demonstrated [25]. $B_1$ mapping in sodium aids with quantitation of sodium which leads to benefits mentioned previously.

• A comparison between a dual-tuned and single-tuned sodium coil is presented [29]. This shows the superior performance of a new dual-tuned coil design which also improves the performance of sodium quantitation.

• A water- and fat-separation technique using multiple acquisition SSFP is described [26]. This has the potential to accelerate imaging of water and fat in MRI. Decrease in scan time directly relates to decreased costs for performing that examination.

• An inter-site and inter-vendor quantitative MRI study is introduced [30]. Inter-site and inter-vendor quantitative studies have the potential to increase the available subjects for study and decrease the cost of those studies because existing infrastructure can be used.

• A relaxation and contrast optimization for laryngeal imaging at 3T is introduced [31]. The specific goal of this study is to optimize contrast for automated segmentation of the larynx. Understanding of the in vivo performance of the larynx is incomplete. With automated segmentation of the larynx, more realistic models can be created which will assist doctors in study and treatment of laryngeal diseases.

• Finally, diffusion imaging with insert gradients is introduced [32]. Diffusion imaging is useful for the study of fibrous tissue deformities but suffers from low SNR. The goal of introducing insert gradients is to increase the SNR in diffusion imaging.
These contributions are many and varied. The link between some of them is not immediately apparent. However, all are based on techniques and skills developed to improve sodium quantitation.
Chapter 2

Magnetic Resonance Imaging Physics Primer

The phenomenon of Nuclear Magnetic Resonance (NMR) was first described by Felix Bloch [7] and Edward Purcell [10] independently in 1946. In that same year, Bloch et al. demonstrated a method to observe it [8]. In 1973, Lauterbur introduced the concept of image formation from the NMR signal [1]. Mansfield and Maudsley improved the concept of Magnetic Resonance Imaging (MRI) by introducing the Fourier transform as a method to understand data acquisition and image reconstruction [3]. Since that time, MRI has been an important medical imaging method because it does not use ionizing radiation and it can generate excellent soft-tissue contrast.

The goal of this chapter is to lay a foundation for understanding how MR images are formed. To begin with, many basic NMR physics concepts are introduced. Next, the hardware of an MRI machine which takes advantage of the NMR physics for imaging is described. Finally, this chapter concludes by tying the physics and hardware together by explaining how MR images are formed.

2.1 Nuclear Magnetic Resonance Physics

One may visualize Nuclear Magnetic Resonance (NMR) of non-ferromagnetic materials by picturing each nucleus as a tiny magnet that is spinning about an imaginary axis between its magnetic poles. Without a magnetic field present, the magnetic moment of each nuclei in a macroscopic sample will have random orientation with respect to each other. This will lead to an effectively zero magnetic field at the macroscopic level as shown in figure 2.1(a).
Figure 2.1: Effect of $\vec{B}_0$ on magnetic moments: (a) depicts a group of magnetic moments in a possible configuration at some instant in time. The vector sum of these magnetic moments in part (a) will be practically zero. In (b), a strong external magnetic field, $\vec{B}_0$, is applied. At any moment in time, some of the magnetic moments will be aligned parallel or antiparallel with the applied magnetic field. There is a bias toward aligning parallel with the applied field which leads to a non-zero net magnetic moment for the sample. Other alignments in the sample are due to thermal (Brownian) motion.

2.1.1 Magnetization

If an external magnetic field, $\vec{B}_0$, is applied, some of the magnetic moments of the nuclei will align parallel with this field while others will align anti-parallel and still others will not be aligned due to thermal (Brownian) motion as depicted in figure 2.1(b). The net effect is a small magnetic moment, $\vec{M}$, aligned with $\vec{B}_0$ on the macroscopic scale. From this point on, the net magnetic moment of a sample will be referred to as, simply, the magnetic moment or magnetization unless otherwise specified.

The direction of the external magnetic field, $\vec{B}_0$, is called the longitudinal direction. The plane normal to the longitudinal direction is the transverse plane.

2.1.2 Bloch Equation

Felix Bloch mathematically described the NMR phenomenon with

$$\frac{\partial \vec{M}}{\partial t} = \vec{M} \times \gamma \vec{B} - \frac{M_x \hat{i} + M_y \hat{j}}{T_2} - \frac{(M_z - M_0) \hat{k}}{T_1}, \quad (2.1)$$
where $\vec{M} = (M_x, M_y, M_z)^T$ is the magnetic moment of a volume, $\gamma$ is constant and a property of the atom being imaged, $\vec{B}$ is the applied magnetic field, $M_0$ is the magnitude of the longitudinal thermal equilibrium state of the net magnetization, $T_1$ and $T_2$ are time constants that depend on the material being observed and are defined in section 2.1.7, and $\hat{i}$, $\hat{j}$, and $\hat{k}$ are unit vectors in the $x$, $y$, and $z$ direction respectively [7].

The terms $\hat{i}$, $\hat{j}$, and $\hat{k}$ are used for simplicity of notation to represent three coupled differential equations in a single equation. By convention, the $z$ or $\hat{k}$ direction is in the longitudinal direction. The $\hat{i}$ and $\hat{j}$ directions are perpendicular to the $\hat{k}$ direction and to each other.

### 2.1.3 Precession

The term $\vec{M} \times \gamma \vec{B}$ in equation 2.1 represents precession which occurs when the magnetization of the sample is out of alignment with the applied magnetic field. This misalignment may result from applying a new field or through perturbation of the magnetization. One method of magnetization perturbation is discussed in section 2.1.5. NMR precession is comparable to the precession of a top: the axis of the spinning top starts to wobble as the top succumbs to gravitational pull. The magnetization is like the axis of the top and the gravitational pull is comparable to the applied magnetic field. The precession frequency is proportional to the strength of the magnetic field and is called the Larmor frequency. This phenomenon will generate a small varying electromagnetic field which can be detected with a specialized detector [8], often referred to as a coil. Precession is illustrated in figure 2.2.

### 2.1.4 Rotating Frame

A static reference frame is often used where all movement is described relative to the static frame. However, for nuclear magnetic resonance, if one considers the frame of reference rotating at the Larmor frequency, the magnetization vector becomes static relative to it [33]. This allows complex motions, such as nutation, to be represented simply as a 3D rotation. Other convenient simplifications are also enabled in the rotating frame. For example, the rotating frame was used to derive the phase accrual caused by the Bloch-Siegert shift used for the Bloch-Siegert shift $B_1$ mapping method in section 3.3.6.
2.1.5 Excitation

Precession only occurs when the magnetization is not in thermal equilibrium. Moving the magnetization out of thermal equilibrium is called excitation. Excitation occurs when a coil transmits a resonance RF field to the magnetization. This excitation field is called the $\vec{B}_1(t)$ field and is ideally orthogonal to $\vec{B}_0$. Excitation induces the motion of nutation in the magnetization as viewed in the lab reference frame as shown in figure 2.3(a). Excitation is most easily understood in the rotating frame because the complex motion of nutation becomes a simple rotation as depicted in figure 2.3(b).

RF pulses on resonance all cause rotation as depicted in figure 2.3. Sometimes they have different purposes than excitation or are more than a single pulse. These different pulses may have different names. However, the theory explained in this section still applies. The terms “compound” or “composite” applied to an RF pulse, just mean that the envelope of the pulse can be thought of as multiple pulses, one right after the other. The term “refocusing” means the pulse is not intended to excite spins. It is intended to undo “$T_2^*$” relaxation (discussed in section 2.1.7). Understanding refocusing pulses is not required for the research presented in this dissertation. The interested reader can find more information.
The $\vec{B}_1(t)$ RF pulse can be decomposed into two components. By decomposing the RF pulse into two components, the analysis can be simplified with lower frequency variations. One component is the frequency of the field which is usually tuned to the resonance, or Larmor, frequency. This is the high frequency component of the RF pulse and can usually be ignored by using the rotating frame for analysis. The other component is the amplitude, or strength, of the field. How the amplitude varies in time is called the envelope of the $\vec{B}_1(t)$ field. Figure 2.4 illustrates the difference between the RF pulse and the RF envelope. The variations of the $\vec{B}_1(t)$ envelope are an order of magnitude slower than the frequency of the $\vec{B}_1(t)$ field. Therefore, amplitude can usually be considered constant with respect to time even though it does vary [33].

Neglecting relaxation, which is discussed in section 2.1.7, equation 2.1 becomes

$$\frac{\partial \vec{M}}{\partial t} = \vec{M} \times \gamma \vec{B}_{1,r},$$  \hfill (2.2)
Figure 2.4: Illustration of an RF envelope: The example RF pulse (a sinc pulse) is shown in blue. The slowly varying change in amplitude shown in black is the RF Envelope.

where $\vec{B}_{1,r}$ is the slowly varying envelope of the RF excitation pulse and is treated as constant with respect to the time differentiation. If $\vec{B}_{1,r} = B_{1,r}\hat{i}$, the solution to equation 2.2 is

$$\vec{M}(t) = -\cos(\gamma B_{1,r}t)\hat{j} + \sin(\gamma B_{1,r}t)\hat{k}. \quad (2.3)$$

This solution is general for any $B_{1,r}$ in the rotating frame of the transverse plane. The phase of the rotating frame can be chosen so that $B_{1,r} = B_{1}\hat{i}$. This shows that application of a resonant $\vec{B}_1$ field in the transverse plane causes a rotation in the plane orthogonal to the field. The degree of this rotation is called the flip angle.

**Relationship Between Flip Angle and $B_1$**

When discussing excitation, there are two related concepts: flip angle and $B_1$ strength. This section discusses how the flip angle and $B_1$ strength are similar measures. Flip angle is often directly related to $B_1$. 

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For a non-selective excitation, flip angle is a simple integration of the on-resonant $B_1$ envelope with respect to time:

\[ \alpha = \int_0^T \gamma B_1(t)dt. \]  

(2.4)

Changing the flip angle is done by changing the strength of the $B_1$ field while leaving the shape of the $B_1$ envelope the same. By mathematically separating the strength of the $B_1$ from the shape if its envelope, the flip angle is related to the $B_1$ strength by a simple scalar multiplier. This separation of the $B_1$ field into its peak value and the normalized envelope is shown with

\[ B_1(t) = B_{1,\text{peak}} \cdot \hat{B}_1(t), \]  

(2.5)

where $B_{1,\text{peak}}$ is the peak value of the $B_1$ pulse and $\hat{B}_1(t)$ is envelope of the RF pulse which is normalized by $B_{1,\text{peak}}$.

Now equation 2.4 may be simplified by substituting equation 2.5 for $B_1(t)$. The result is that the flip angle and $B_{1,\text{peak}}$ are proportional with

\[ \alpha = B_{1,\text{peak}} \cdot K_{\text{ex}}, \]  

(2.6)

where

\[ K_{\text{ex}} = \int_0^T \gamma \hat{B}_1(t)dt. \]  

(2.7)

Equation 2.6 is why the terms flip angle and $B_1$ can usually be interchanged. This applies to non-selective excitation. With selective excitation the relationship is approximately proportional for small flip angles. However, flip angle and $B_1$ are different when using selective excitation (discussed in section 2.1.6).

### 2.1.6 Selective Excitation

A specialized subset of excitation is called selective excitation. Selective excitation is a technique that allows a reduction of the imaging volume which directly reduces the imaging time. Non-selective RF excitation induces signal inside everything that receives RF power.

Selective excitation is illustrated in figure 2.5. Selective excitation relies on RF pulses only exciting a finite set of frequencies and using magnetic fields to induce changes in the
Larmor frequency that vary with position so that the specific set of frequencies excited correspond to the Larmor frequencies in the desired excitation area. That sounds complicated so it will be broken down into different steps. First, consider the RF pulse in figure 2.5(a). Each RF pulse carries power at specific frequencies. The frequencies an RF pulse carries power at can be calculated using a Fourier transform as shown in figure 2.5(b). This frequency representation of the RF pulse roughly approximates the level of excitation to each nucleus at that Larmor frequency. The magic of selective excitation occurs by applying a spatially varying magnetic field across the volume. This causes the Larmor frequency to vary with position. Figure 2.5(c) demonstrates the mapping of Larmor frequency to position with $\gamma$, the gyromagnetic ratio, relating the spatially varying static magnetic field to the spatially varying Larmor frequency in figure 2.5(d). Excitation occurs where the Larmor frequency of nuclei in the object match where there is power in the RF spectrum. This is only an approximation and may introduce errors in quantitative imaging that is discussed further in chapter 5. However, in many imaging scenarios this is an excellent approximation.

2.1.7 Relaxation

Excitation causes a perturbation of the thermal equilibrium. The return to thermal equilibrium is described accurately in most cases by two relaxation mechanisms. The first mechanism relates to how quickly the net magnetization returns to thermal equilibrium. It originates from the term $-(M_z - M_0) \hat{k}/T_1$ in equation 2.1. If we assume $\vec{B}$ is entirely in the longitudinal direction, equation 2.1 becomes

$$\frac{\partial M_z}{\partial t} = -\frac{(M_z - M_0) \hat{k}}{T_1}. \quad (2.8)$$

The solution is

$$M_z(t) = M_0 + (M_z^i - M_0) e^{-t/T_1}, \quad (2.9)$$

where $M_z^i$ is the initial longitudinal magnetization and $t$ is the time relative to the time of the initial magnetization. This exponential recovery happens in the longitudinal direction and is defined by the time constant $T_1$. An example of this behavior is shown in figure 2.6(a). The origins of $T_1$ relaxation are nuclear spins exchanging energy with their surroundings.
Figure 2.5: Illustration of selective excitation: Selective excitation is illustrated starting with the $B_1$ (RF) pulse envelope in part (a). Part (b) represents the frequency components of the excitation pulse calculated with the Fourier transform. The frequency of the RF pulse is related to varying Larmor frequency in part (c) which is proportional to the static spatially varying magnetic field in part (d) which all combine to create selective excitation.

The second mechanism is transverse relaxation with a time constant $T_2$. $T_2$ relaxation relates to dephasing in the transverse plane due to the random motion of molecules. It is an exponential decay as shown in figure 2.6(b). It originates from the term $-(M_x \hat{i} + M_y \hat{j})/T_2$ in equation 2.1. By focusing on this term, without loss of generality equation 2.1 becomes

$$\frac{\partial \vec{M}}{\partial t} = -\frac{M_x \hat{i} + M_y \hat{j}}{T_2}. \quad (2.10)$$

The solution is simple exponential decay expressed as

$$\vec{M}_{xy}(t) = \vec{M}_{xy}^i e^{-t/T_2}, \quad (2.11)$$

where $\vec{M}_{xy} = M_x \hat{i} + M_y \hat{j}$ and $\vec{M}_{xy}^i$ is the magnetization in the transverse plane at the beginning of the time period. The origin of $T_2$ relaxation is the dephasing due to instantaneous changes in the local magnetic field of each nuclear spin.
Figure 2.6: Illustration of relaxation effects: The time constant $T_1$ describes the longitudinal recovery of the signal to thermal equilibrium as illustrated in (a). The time constant $T_2$ describes the exponential decay of the signal in the transverse plane after signal excitation illustrated in (b).

$T_1$ and $T_2$ relaxation are both random processes and irreversible. There is another mechanism that appears similar to $T_2$ called $T_2^*$ decay. It is a combination of $T_2$ decay along with decay due to slight variations in the magnetic field that each nucleus interacts with. The decay from variations in the magnetic field cause a deterministic dephasing of the signal which may be reversed [34].

2.1.8 Noise in MRI

The primary source of noise in MRI is the Brownian (thermal) noise of electrons found in conductors. This is often called Johnson (resistive) noise. This noise originates from the movement of electrons in the body and the movement of electrons in the components of the receiver coil. However, the dominant source of Johnson noise in an MR imaging experiment is usually the body of the subject being imaged. This noise is modeled accurately by a bivariate Gaussian distribution with a uniform power spectral density (white noise) [35].

2.2 Hardware

Foundations in NMR physics were presented in section 2.1. In this section, the major hardware components of an MRI machine will be introduced. These hardware components are utilized to induce and manipulate magnetization in a sample. In this section, a description of how these hardware components manipulate the magnetization of a sample will be
delineated. In section 2.3, a description of how images are formed using these magnetization manipulations will be presented.

There are three basic hardware components of an MRI machine: (1) A superconducting electromagnet to generate a strong static magnetic field that polarizes the nuclear magnetic moments; (2) One or more specialized coils to induce precession and receive the resulting signal; and (3) three separate electromagnets that produce linearly varying magnetic fields in the $x$, $y$, and $z$ directions respectively. The following is a brief introduction to each hardware component with its purpose.

### 2.2.1 The Static Magnetic Field ($\vec{B}_0$)

Typically, the static magnetic field $\vec{B}_0$ which polarizes the nuclear magnetic moments is generated with a superconducting solenoid electromagnet. A solenoid is generally used because they generate a homogeneous magnetic field down the axis of the hollow cylindrical bore. Magnetic fields used for imaging are typically in the range of 1.5-3 Tesla which is 3-6000 times stronger than the earth's magnetic field. Superconducting materials are usually used because the power required to generate magnetic fields that strong are astronomical; in standard resistive wires, the heat generated by that much power would be prohibitive. $\vec{B}_0$ is used to polarize a portion of the nuclei inside it. The stronger the magnetic field, the larger the proportion of nuclei that are aligned. Greater numbers of aligned nuclei correspond to a higher signal to noise ratio (SNR). Higher SNR means a finer image resolution can be acquired or techniques for functional imaging that were impractical at lower SNR can be achieved. A stronger magnetic field also means a higher Larmor frequency which also improves the SNR of some types of coils.

### 2.2.2 The Radio Frequency Field ($\vec{B}_1$)

Aligned nuclei are not beneficial for imaging by themselves. Nuclei in thermal equilibrium produce no signal that can be detected. That is where the radio frequency (RF) field comes in. A specialized detector, or coil, is used to generate this field. The RF field perpendicular (transverse) to the static magnetic field perturbs, or tips, the magnetization. This is called excitation. Once the magnetization is tipped, the same or different RF coil can
receive signal from the nuclei as they precess back into alignment with the static magnetic field. Signal is most effectively received perpendicular to the static magnetic field.

2.2.3 The Linear Magnetic Field Gradients \((G_x, G_y, G_z)\)

With all the nuclear magnetic moments polarized and then excited, there is no way to determine the strength of the signal in a specific location. That means even though everything may be giving off signal, there is no way to tell signal at one point from signal at another point. This is where linear magnetic field gradients come in. A linear gradient applied to the imaging volume creates a difference in the resonance frequencies that is dependent on the strength of the gradient. With nuclear magnetic moments precessing at frequencies that are dependent on position, the signal can be differentiated spatially by resolving the signal strength based on frequencies. This effect is utilized to localize signal and form an image. An ideal gradient for typical imaging generates a magnetic field that is always oriented parallel with \(\vec{B}_0\) and varies linearly in a single direction. There are three linear gradients oriented orthogonal to each other. This will be discussed in more detail in Section 2.3.

2.3 Image Formation

The MRI phenomenon and hardware introduced in the previous sections can be used to form images. The basic idea behind image formation is creating frequency variations based on position which allow signal to be localized.

2.3.1 k-space

The time-domain data before Fourier transformation is called k-space. This is the space MRI images are sampled in. An alternate name is Fourier space because a common method of reconstruction is a 2D or 3D Fourier transform.

2.3.2 Trajectory

The method k-space is traversed and sampled can be manipulated. The order that an MRI image is sampled is called the trajectory. A common method for sampling k-space is to
scan it line-by-line on a Cartesian grid. When sampling is done this way, the reconstruction is a simple 3D fast Fourier transform (FFT). Efforts to image cardiac muscle in real time (faster imaging) or cortical bone and ligament (imaging with less delay between excitation and reception) have lead to different sampling trajectories. Many start sampling before any gradients are applied and then sample out radially, either straight or in a spiral. This may be done in 2- or 3-dimensions.

Sampling on a Cartesian grid is the “gold standard” trajectory for two reasons: the artifacts are well understood; and reconstruction using the FFT algorithm is the fastest method of reconstruction available. Reconstruction of data sampled using a non-Cartesian trajectory could be done with a direct Fourier transform. However, that method is impractical due to the time reconstruction would take. Typically, reconstruction for data acquired on a non-Cartesian grid utilizes an algorithm to estimate what the data would be on a Cartesian grid. That process is often called regridding. Following the regridding, an FFT is used to complete the reconstruction.

2.3.3 Frequency Encoding

An RF coil can receive the signal generated by precession. However, a single RF coil cannot differentiate signal based on the physical position the signal is coming from. Frequency encoding is one method of determining the strength of the signal based on the position the signal is coming from. It works by applying a constant magnetic field gradient during the readout that causes a variation in magnetic field across the object being imaged. The strength of the magnetic field at any point within the object is proportional to its position. Differences of magnetic field cause a variation in frequency across the object being imaged. After signal reception, the data is then decomposed into its frequency components. The frequency components of the signal map directly to different positions in the object. Figure 2.7 represents this process with an illustration. This process allows the image to be reconstructed in one dimension. There are still one or two dimensions that need to be resolved, depending on if a 2D or 3D image is being acquired. Section 2.3.4 describes how the other direction(s) are resolved.
**2.3.4 Phase Encoding (2D and 3D)**

Frequency encoding only works in one direction at a time. The other one or two orthogonal directions can be encoded using a similar principle. However, instead of continuously sampling during the time that a gradient is applied, gradients are applied at a fixed amplitude and for a fixed duration before the acquisition. This generates a phase variation that is position dependent. Through repeating this process multiple times, you effectively sample phase changes over time – digitally sampling a time evolution of various frequencies. The phase encoding is applied in two directions for 3D imaging and one direction for 2D imaging with frequency encoding sampling the remaining direction. With all directions having the position encoded in the frequency content, a Fourier Transform of the acquired signal is an image of the object.
2.3.5 Repetition Time (TR)

A simple implementation of phase encoding requires the pulse sequence to be repeated once for each sample required in the phase encode direction. The time between repetitions is called the repetition time, or TR.

2.3.6 Echo Time (TE)

An “echo” in MRI is when the center of k-space is crossed. This can be the absolute center of all axes or offset from the center in one or two directions and crossing the center in at least one direction. The position in k-space is typically manipulated with the use of the gradients. However, a special type of RF pulse conjugates the position in k-space. When this special type of pulse is used to conjugate the k-space position, the resulting echo is called a spin echo. A spin echo also has the special property of reversing $T_2^*$ decay in order to measure pure $T_2$ decay. All other echoes are called gradient echoes or gradient recalled echoes (GRE). Echo time is the effective time between excitation and when the echo occurs.

2.3.7 Pulse Sequence Diagram (PSD)

A pulse sequence diagram is a concise way to represent the timing of an MRI pulse sequence. Often represented are: RF pulse timing and envelope shape, timing of acquisition or ADC, and timing of gradients. The most simple pulse sequences neglect everything except the timing and envelope shape of the RF pulse.
## Table 2.1: Definitions of Commonly Used MRI Terms and Acronyms

<table>
<thead>
<tr>
<th>MRI Term</th>
<th>Brief Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>$B_0$</td>
<td>Main static magnetic field oriented in the longitudinal direction.</td>
</tr>
<tr>
<td>$B_1$</td>
<td>RF field used for excitation and reception of signal.</td>
</tr>
<tr>
<td>$T_1$</td>
<td>Longitudinal magnetization exponential recovery time constant.</td>
</tr>
<tr>
<td>$T_2$</td>
<td>Transverse magnetization exponential decay constant.</td>
</tr>
<tr>
<td>$T_2^*$</td>
<td>Transverse magnetization exponential decay constant which includes reversible dephasing effects.</td>
</tr>
<tr>
<td>TR</td>
<td>Repetition time: time between repetitions of the pulse sequence.</td>
</tr>
<tr>
<td>TE</td>
<td>Echo time: time between effective excitation and sampling of the center of k-space.</td>
</tr>
<tr>
<td>k-space</td>
<td>The space in which MRI images are sampled. Also called Fourier space.</td>
</tr>
<tr>
<td>PSD</td>
<td>Pulse sequence diagram: a shorthand method for representing how the MRI hardware is used to produce an image.</td>
</tr>
<tr>
<td>Echo</td>
<td>Crossing the center of k-space in at least one direction.</td>
</tr>
<tr>
<td>GRE</td>
<td>Gradient recalled echo. Anything echo that is not a spin echo.</td>
</tr>
<tr>
<td>Spin Echo</td>
<td>An echo induced by a special RF pulse that conjugates the position in k-space.</td>
</tr>
<tr>
<td>pixel</td>
<td>Picture (pix) element (el). One “dot” in a 2D MRI image.</td>
</tr>
<tr>
<td>voxel</td>
<td>Volume (vox) element (el). The resultant signal from a single element in the 3D volume.</td>
</tr>
</tbody>
</table>
Chapter 3

$B_1$ Mapping Primer

The general idea behind $B_1$ mapping is to determine a pulse sequence that varies with respect to the $B_1$ field and only the $B_1$ field. MR image signal intensity depends on many variables, a single acquisition is not enough to uniquely quantify the $B_1$ field. Therefore, at least two images are usually acquired and a mathematical operation is used to cancel out all other undesired characteristics in the image.

In this dissertation the term “$B_1$ mapping” refers to both methods that directly estimate the $B_1$ field and methods that indirectly estimate the $B_1$ field through the flip-angle which is a function of $B_1$ field strength. Flip-angle is a measure of signal intensity variations due to the transmit $B_1$ field. Knowledge of the flip-angle is generally the desired outcome from $B_1$ mapping so those intensity variations can be accounted for. However, the relationship between flip-angle and $B_1$ is much more complex in cases of slab-selection and slice-selection.

There are two general categories of $B_1$ mapping: magnitude-based and phase-based. They are categorized on whether the magnitude or phase of the image is used to estimate the $B_1$. There is some cross over between phase and magnitude methods (e.g., Insko and Bolinger [16] use a ratio of magnitudes of two images to determine the flip-angle and use the phase of the images to extend the range where the method would be ambiguous without it). However, most methods are predominantly phase-based or magnitude-based.

3.1 Magnitude-Based Methods

Magnitude-based methods estimate the $B_1$ from the magnitude of the image. They originated in 1987 with two papers [13, 14]. Axel et al. introduced a method of image intensity correction by estimating the relative $B_1$ field using a uniform phantom. Murphy-
Boesch et al. [14] introduced a method of $B_1$ mapping which required specialized equipment and measured the nutation rate of the spins in the presence of the $B_1$ field. A couple more popular magnitude-based methods are the Dual-Angle (DA) method and the Actual Flip-Angle Imaging (AFI) method introduced by Insko and Bollinger in 1993 [16] and Yarnykh in 2007 [17] respectively.

3.2 Phase-Based Methods

Phase-based methods estimate the $B_1$ from the phase of the image. The first phase-based method was introduced by Oh et al. [15] in 1990, referred to in this dissertation as the Spin Echo Phase-Sensitive (SEPS) method. The SEPS method uses a compound spin echo pulse to encode the flip-angle in the phase of the resulting image. In 2008, Morrell introduced the Phase-Sensitive method [18]. Instead of using a spin echo sequence, Morrell uses a compound excitation pulse with a gradient echo sequence to encode the flip-angle in the phase of the resulting image. Sacolick et al. [36] introduced the Bloch-Siegert Shift method in 2010 which has garnered significant interest.

The main reason the Bloch-Siegert shift method has had so much interest since being introduced is because of its potential with parallel transmit MRI. Chapter 1 mentions that parallel transmit MRI is an active area of research right now because of the inhomogeneity problem it can help solve in high-field MRI systems. The Bloch-Siegert shift method has been heavily involved in the recent high-field MRI research.

3.3 Description of Six $B_1$ Mapping Methods

This section presents the basic techniques for five important $B_1$ mapping methods:

- the uniform phantom-based method;
- the GRE-Dual-Angle $B_1$ mapping method;
- the Actual Flip-Angle Imaging (AFI) method;
- the SEPS method;
- the Phase-Sensitive (PS) method;
• the Bloch-Siegert Shift (BSS) method.

The uniform phantom-based method and the SEPS method of $B_1$ mapping are described to give context for the different available methods. The remaining methods described in this chapter will be referenced in later chapters, so a basic understanding is important for comprehension of the presented research findings.

3.3.1 Uniform Phantom-Based Method

Axel et al. [13] introduced a $B_1$ mapping method that does not allow for absolute measurement of the $B_1$ field. It produces relative measurements that are adequate for certain non-quantitative circumstances. This method uses the image intensity from a uniform phantom scan and normalizes it as an estimate for the relative $B_1$ map. Using the one phantom scan, the relative $B_1$ map is then used for other scanning scenarios to reduce the variation in image intensity due to coil profile effects. It is a simple and straightforward technique to use. However, the relative map does not account for tissue specific effects and coil loading for in vivo imaging.

3.3.2 Gradient Recalled Echo Dual-Angle $B_1$ Mapping Method

The gradient recalled echo dual-angle (GRE-DA) $B_1$ mapping method uses the magnitude of two images: one acquired at a nominal flip-angle of $\alpha$ and another acquired at a nominal flip-angle of $2\alpha$ with signal magnitudes of

$$m_1 = M_0 \sin(\alpha)$$  \hspace{1cm} (3.1)

and

$$m_2 = M_0 \sin(2\alpha)$$ \hspace{1cm} (3.2)

respectively. $M_0$ denotes the magnitude of the thermal equilibrium magnetization. Other sources of variations in image magnitude are removed by forming the ratio of these two images,

$$r = \frac{m_1}{m_2} = \frac{1}{2 \cos \alpha}.$$ \hspace{1cm} (3.3)
This ratio of image magnitudes is used to estimate \( \alpha \) [16].

The GRE-DA \( B_1 \) mapping method is inherently an image magnitude-based method. Image magnitude has a dependence on \( T_1 \) that is not modeled accurately with equation 3.3 unless complete \( T_1 \) recovery is achieved with a long TR or saturation recovery (e.g., Cunningham et al. [37]). If \( T_1 \) effects are not eliminated by long TR or saturation recovery, an additional mean bias will be introduced into the \( B_1 \) estimate.

The pulse sequence used to generate the images for this version of the DA method is a basic GRE pulse sequence as shown by the pulse sequence diagram (PSD) in figure 3.1.

### 3.3.3 Actual Flip-Angle Imaging Method (AFI)

The Actual Flip-Angle Imaging (AFI) method utilizes a dual-steady-state signal and the ratio of those signals, \( r = S_2/S_1 \) where \( S_1 \) is the signal from the first TR and \( S_2 \) is from the second TR, to determine the flip-angle. The dual-steady-state is achieved with two
repetition times (TR) that alternate, TR\(_1\) and TR\(_2\). The second TR, TR\(_2\), is greater than the first TR, TR\(_1\). The ratio of both TRs is defined as \( n = \frac{\text{TR}_2}{\text{TR}_1} \). The ratio of the steady-state signals is approximately

\[
r \approx \frac{1 + n \cos(\alpha)}{n + \cos(\alpha)}.
\] (3.4)

Solving for the flip-angle,

\[
\alpha \approx \arccos \left( \frac{rn - 1}{n - r} \right).
\] (3.5)

The pulse sequence diagram for the AFI method is shown in figure 3.2.

3.3.4 Spin Echo Phase-Sensitive (SEPS) Method

The Spin Echo Phase-Sensitive (SEPS) method introduced by Oh et al. [15] uses a compound-refocusing pulse to encode the \( B_1 \) in the phase of the image acquired. Two
acquisitions are still required to negate non-desired phase differences. The pulse sequence has a standard selective excitation followed by a non-selective compound-refocusing pulse, $90_y - 180_x - 90_y$, to form a spin echo [34]. The second acquisition is identical except the compound-refocusing pulse is $90_y - 0_x - 90_y$ where the $0_x$ is a time gap equal to the length of the $180_x$ in the first acquisition. Figure 3.3 shows the pulse sequence diagram for this pulse sequence.
3.3.5 Phase-Sensitive Method (PS)

The Phase-Sensitive (PS) $B_1$ mapping method uses a composite-excitation pulse of $2\alpha_y-\alpha_x$ to generate phase in the image which varies with flip-angle. Measurement of this phase allows estimation of flip-angle. Other sources of image phase are removed by taking the phase difference of two acquisitions, one with the $2\alpha_y$ pulse sign reversed. Equations for the magnetization after the composite-excitation pulse of the PS method are

\[
M_x = \pm \frac{M_0 \alpha \Delta \omega \tau}{\beta^2} [4 \sin^2(\beta) \cos(\beta)] \\
- \frac{M_0 \alpha \sin \beta}{\beta^3} [\alpha^2 \cos(2\beta) + \Delta \omega^2 \tau^2], \quad (3.6)
\]

\[
M_y = \pm \frac{M_0 2 \alpha \sin(\beta)}{\beta^3} [\Delta \omega^2 \tau^2 \cos(2\beta) + \alpha^2 \cos(\beta)] \\
+ \frac{M_0 \alpha \Delta \omega \tau}{\beta^4} [1 - \cos(\beta)][\alpha^2 \cos(2\beta) + \Delta \omega^2 \tau^2], \quad (3.7)
\]

\[
M_z = \pm \frac{2M_0 \alpha^2 \Delta \omega \tau \sin(\beta)}{\beta^3} [\cos(\beta) - \cos(2\beta)] \\
+ \frac{M_0 \alpha^2 \cos(2\beta) + \Delta \omega^2 \tau^2}{\beta^4} [\alpha^2 \cos(\beta) + \Delta \omega^2 \tau^2], \quad (3.8)
\]

where $\beta = \sqrt{\alpha^2 + \Delta \omega^2 \tau^2}$, $M_0$ is the thermal equilibrium magnetization magnitude, $\Delta \omega$ is the off-resonance frequency, and $\tau$ is the duration of the $\alpha_x$ hard pulse. The $2\alpha_y$ flip is achieved with a hard pulse which is double the length of the $\alpha_x$ pulse while maintaining equal magnitude, and $\pm$ represents the sign of the $2\alpha$ flip [18].

As seen in equation 3.6-equation 3.8, flip-angle estimation with the PS method is affected by off-resonance ($\Delta \omega$). For modest $B_0$ inhomogeneity, this effect contributes only minimally to the flip-angle estimate and can be ignored (e.g., Allen et al. [25]). In situations with higher $B_0$ inhomogeneity, the effect of off-resonance can be corrected with a $B_0$ map, which somewhat increases scan time. With severe $B_0$ inhomogeneity, the PS method can fail altogether for some ranges of flip-angles. The pulse sequence diagram for the PS method is shown in figure 3.4.
Figure 3.4: Phase-sensitive method pulse sequence diagram: The PS method uses a GRE pulse sequence with a compound excitation pulse as shown by this pulse sequence diagram.

3.3.6 Bloch-Siegert Shift Method (BSS)

The BSS $B_1$ mapping method exploits the fact that the application of an off-resonance RF pulse slightly changes the effective frequency of spins that are on resonance [38]. The slight difference in effective frequency causes the previously excited magnetization to gain phase over the duration of the RF pulse. The total phase accrual is proportional to the RF pulse energy and inversely proportional to the off-resonance frequency. Specifically, the phase $\phi_{\text{BSS}}$ imparted to the transverse magnetization by the Bloch-Siegert RF pulse is described
by
\[ \phi_{\text{BSS}} = \int_0^T \omega_{\text{BSS}}(t) dt, \] (3.9)

where
\[ \omega_{\text{BSS}}(t) = -\Delta \omega_{\text{RF}}(t) + \sqrt{\Delta \omega_{\text{RF}}^2(t) + (\gamma B_1(t))^2} \] (3.10)
\[ \approx \frac{(\gamma B_1(t))^2}{2 \Delta \omega_{\text{RF}}(t)}, \quad \text{for } \Delta \omega_{\text{RF}}(t) \gg \gamma B_1(t). \] (3.11)

The off-resonance frequency \( \Delta \omega_{\text{RF}}(t) \) of the BSS pulse is defined relative to the Larmor frequency, and \( B_1(t) \) represents the magnetic field strength of the BSS pulse. This expression can be simplified, as noted in chapter 2, by defining the time-varying RF field strength \( B_1(t) \) as the product of the maximum \( B_1 \) amplitude, \( B_{1,\text{peak}} \), and the normalized RF waveform \( \hat{B}_1(t) \). Then the BSS phase can be defined in terms of \( B_{1,\text{peak}} \) and a constant, \( K_{\text{BSS}} \), which fully describe the RF waveform’s potential for creating BSS phase shift:

\[ \phi_{\text{BSS}} \approx \int_0^T \frac{(\gamma B_1(t))^2}{2 \Delta \omega_{\text{RF}}(t)} dt = B_{1,\text{peak}}^2 \int_0^T \frac{(\gamma \hat{B}_1(t))^2}{2 \Delta \omega_{\text{RF}}(t)} dt = B_{1,\text{peak}}^2 \cdot K_{\text{BSS}}, \] (3.12)

where
\[ K_{\text{BSS}} = \int_0^T \frac{(\gamma \hat{B}_1(t))^2}{2 \Delta \omega_{\text{RF}}(t)} dt \] (3.13)

and \( T \) is the period of time the BSS pulse is applied. Note that the rotation \( \phi_{\text{BSS}} \) occurs approximately about the axis of the \( B_0 \) field when \( \Delta \omega_{\text{RF}} \gg B_{1,\text{peak}} \). However, the actual rotation axis may be modeled with methods detailed by Rabi et al. [33]. Rabi et al. [33] models the off-resonance frequency, \( \Delta \omega_{\text{RF}} \), as a vector coaxial with the \( B_0 \) field and the \( B_1 \) field strength as a vector in the transverse plane with magnitude \( \gamma B_1 \). The sum of these two vectors is the axis of rotation. This vector sum may vary greatly from the axis of the \( B_0 \) field when the condition \( \Delta \omega_{\text{RF}} \gg B_{1,\text{peak}} \) is not satisfied, in which case the approximation given in equation 3.11 no longer holds.

The \( B_{1,\text{peak}} \) estimate is formed from the phase difference of two acquisitions, with the off-resonance frequency of the BSS pulse set to \( \pm \Delta \omega_{\text{RF}} \) to eliminate other sources of phase in the image [36].
The BSS method uses two RF pulses. The first is a conventional RF excitation which creates the transverse magnetization. The second is the off-resonance BSS pulse which creates the incremental phase in the transverse magnetization on which $B_1$ estimation is based. These pulse shapes can be chosen independent of each other. Once both pulse shapes are fixed, and assuming the same coil is used for excitation and the BSS pulse, they will scale proportionally to each other as the maximum voltage for each pulse is varied.

**Optimal choice of RF waveform for Bloch-Siegert Shift $B_1$ Mapping Method:** As shown in equation 3.9 and equation 3.11, the phase difference created by the BSS RF pulse is proportional to the integral of the pulse amplitude squared and inversely proportional to the off-resonance frequency of the BSS pulse. $B_1$ estimation will have improved accuracy when the spread of measured phase with respect to variation in $B_{1,\text{peak}}$ is maximized; i.e., by using a BSS pulse with the largest possible energy at the lowest possible off-resonance frequency. BSS pulse energy is limited in practice by specific absorption rate (SAR). The BSS pulse frequency needs to be far enough off-resonance that no excitation occurs. However, recent work has improved the BSS method through novel RF pulse design [39, 40, 41], pulse sequence modification [42, 43, 44], and applying more efficient readout schemes [45].

**SAR constraints on BSS pulse:** Accuracy of $B_1$ estimation improves with the energy of the BSS pulse, but in practice this is limited by SAR considerations. SAR constraints vary widely depending on main field strength, patient weight, and the RF coil being used. However, some recent work has explored mitigating SAR constraints. In general, larger pulse energy requires longer sequence repetition time (TR) in order to keep SAR within safe limits.

**Constraints on the BSS pulse off-resonance frequency:** Minimizing the off-resonance frequency of the BSS pulse maximizes $\phi_{\text{BSS}}$, thereby maximizing the accuracy of $B_1$ estimation. This was demonstrated by Duan et al. [46] in 2013. The minimum off-resonance is constrained by the requirement that the BSS pulse must not cause excitation at the on-resonance frequency. To allow the smallest possible off-resonance frequency without creating excitation on-resonance, the BSS pulse should have a very narrow transition band between the stopband (frequency range with nearly zero energy) and passband (frequency range with
majority of energy) of its frequency spectrum. No matter how small the transition band, off-resonance is limited by the range of $B_0$ homogeneity expected in the experiment. In general, the BSS off-resonance frequency must be at least equal to the maximum expected frequency deviation from the Larmor frequency due to chemical shift, $B_0$ inhomogeneity, the width of the pulse’s transition band, and half passband.

As the BSS pulse approaches on-resonance, the transverse magnetization is partially rotated out of the $M_{xy}$ plane. This leads to variations in the magnitude of the transverse magnetization (i.e., variable signal intensity) and makes the relationship between the accumulated phase and $B_{1,\text{peak}}$ more complicated. The off-resonance pulse can get as close as possible to the resonance and in that case one has to find more accurate ways to estimate $B_1$ from BSS phase shift than equation 3.11 and equation 3.12. The minimization of off-resonance frequency is also limited by the approximation in the relationship between the accumulated phase $\phi_{\text{BSS}}$ and the BSS RF pulse expressed in equation 3.11 and equation 3.12.

The approximation in equation 3.11 and equation 3.12 is based on the assumption that $\Delta \omega_{\text{RF}} \gg \gamma B_1(t)$. When the $\Delta \omega_{\text{RF}}$ is decreased to the point where this assumption is invalid, a more accurate way to estimate the expected BSS phase must be used, such as Bloch simulations. The pulse sequence diagram for the BSS method is shown in figure 3.5.

Even if the Larmor frequency is outside the passband, there will still be a small residual excitation component from the BSS pulse. This may be mitigated without affecting the prepared magnetization by surrounding the BSS pulse with specially designed gradients. The gradient before the pulse is designed to dephase the magnetization. The gradient after the pulse is designed to rephase the magnetization [41]. This leaves magnetization that was excited before the pulse unchanged—everything that was dephased before becomes rephased after. Any magnetization that was not present before the BSS pulse will end up being dephased from the gradient after the pulse since the newly excited magnetization needs no rephasing.

3.4 Conclusion

Some $B_1$ mapping methods use the phase of an image to estimate the $B_1$, such as the BSS, PS, and SEPS methods. Others use the magnitude of an image to estimate $B_1$ such
Figure 3.5: Bloch-Siegert shift method pulse sequence diagram: The BSS method uses a GRE pulse sequence with an additional BSS pulse as shown by this pulse sequence diagram.

as the uniform phantom based method, the DA method, and the AFI method. Six methods are introduced in this chapter. The uniform phantom based method and the SEPS method are introduced to provide context for a greater range of $B_1$ mapping methods. The BSS, PS, DA, and AFI methods are described to provide a basis of understanding in the following chapters.
Chapter 4

A Statistical Analysis of the Bloch-Siegert Shift $B_1$ Mapping Method

4.1 Abstract

A number of $B_1$ mapping methods have been introduced. A model to facilitate choice among these methods is valuable, as the performance of each technique is affected by a variety of factors, including SNR of the constituent images. The Bloch-Siegert Shift $B_1$ mapping method has recently garnered significant interest in the literature because of its utility in parallel transmit MRI. In this chapter, a statistical model suitable for analysis of the Bloch-Siegert Shift method is presented. Unlike previously presented models (e.g., [47]), the analysis is valid in both low-SNR and high-SNR regimes. A detailed analysis of the performance of the Bloch-Siegert Shift $B_1$ mapping method across a broad range of acquisition scenarios is presented, and compared to two other $B_1$ mapping techniques (the Dual-Angle method and the Phase-Sensitive Method). Further validation of the model is presented through both Monte Carlo simulations and experimental results. The simulations and experimental results match the model well, lending confidence to its accuracy. Each technique is found to perform well when the images used to form the $B_1$ maps have high SNR. However, the results suggest that the Dual Angle method is not reliable in low-SNR environments. Furthermore, the Phase-Sensitive method appears to outperform the Bloch-Siegert Shift method in low-SNR cases, although variations of the Bloch-Siegert method may be possible that improve its performance at low-SNR. This chapter demonstrates a technique for analyzing $B_1$ mapping methods that can be used to inform choice among $B_1$ mapping methods, particularly for quantitative measures.
4.2 Introduction

Variations in the radio frequency (RF) transmit field, or $B_1$ inhomogeneity, are a confounding factor for many different magnetic resonance imaging pulse sequences and applications. $B_1$ inhomogeneity results in flip angle variations across the imaging volume, leading to image intensity variations, errors in $T_1$ and other quantitative measurements [48, 49, 50, 51], errors in actual RF waveforms resulting in degraded excitation profiles (e.g., in parallel transmission [52, 53, 54]), and other undesired consequences. Rapidly producing accurate maps of the non-uniform $B_1$ field is an active area of research. These $B_1$ maps can then be used to correct errors in $T_1$ measurement or other quantitative MRI methods and are also necessary for the design of RF pulses for parallel transmission.

Several $B_1$ mapping techniques have been proposed [18, 37, 16, 55, 56, 17], but the relative performance of each technique across a range of conditions is not well understood. A thorough analysis of each method would facilitate choice among them. Such an analysis was recently conducted by Morrell and Schabel [28] for five promising $B_1$ mapping techniques, including comparisons of mean bias and standard deviation of flip angle estimate across a range of basic measurement signal-to-noise ratios (SNRs). More recent work compared the efficacy of dual-angle $B_1$ mapping with Morrell’s Phase-Sensitive method in the low-SNR environment of sodium imaging, validating some of Morrell and Schabel’s [28] previous analysis [25]. Since that analysis Sacolick et al. [36] have introduced the Bloch-Siegert shift (BSS) method of $B_1$ mapping, which has garnered significant interest and yielded promising results. An analysis including the BSS method was done by Pohmann et al. [47] with a focus on the challenges of imaging at 7T. However, the choice of parameters used in their implementation severely limited the signal-to-noise ratio (SNR) efficiency of the methods that usually require longer repetition time (i.e., the Phase-Sensitive method and the dual-angle method), limiting the applicability of the analysis. Therefore, a thorough analysis with optimal implementation of both the BSS and other methods has not yet been conducted.

The work of Morrell and Schabel [28] compared five different $B_1$ mapping methods: the Phase-Sensitive (PS) method [18]; the gradient recalled echo dual-angle (GRE-DA) method [37, 16, 55, 56]; an extended DA method [16]; the actual flip angle imaging (AFI)
method [17]; and an extended AFI method [28]. They show that the PS method performs better in terms of lower standard deviation and mean bias than the other methods analyzed.

In this study, the statistical framework used in [28] is adapted to analyze the performance of the BSS method, and compare it to the performance of both the PS and GRE-DA methods. In Chapter 3 a foundation was laid for the techniques discussed here. A presentation is made of the theoretical derivation and statistical analysis of each technique, followed by a Monte Carlo simulation to validate theory. Finally, quantitative experimental measurement data is provided to validate the model and analysis. The statistical model is shown to be consistent with both the Monte Carlo simulations and experimental results, which gives confidence in the model’s accuracy. With confidence in the models accuracy, the performance of each technique (as measured by mean bias and standard deviation of flip angle estimate) across a range of basic measurement SNRs is then summarized using those models. The phase-based methods (BSS and PS) perform better in low-SNR environments than the DA method as measured by lower mean bias and lower standard deviation of noise. The PS method consistently performs the best in low-SNR environments.

4.3 Theory

The PS and GRE-DA methods are included in this analysis as a phase-based and a magnitude-based reference point to the previous analysis of Morrell and Schabel [28]. While the GRE-DA method is magnitude-based, the PS and BSS methods treated in this study are phase-based. Other methods could be included. However, the focus of this research is to explore the Bloch-Siegert $B_1$ mapping technique. The framework used here is straightforward to extend to other $B_1$ mapping methods, but is beyond the scope of this research.

In Chapter 3, a subtle difference between $B_1$ mapping and flip angle mapping was mentioned. However, here a couple of the differences are mentioned before going into the similarities. Generally, the flip angle is considered proportional to the $B_1$ strength as presented in chapter 3. That is based on the assumption of a uniform magnetic field and on-resonant excitation. If there are imperfections in the main magnetic field ($B_0$), localized environmental variations (e.g., chemical shift), or a gradient applied during excitation, those factors need to be considered when relating flip angle to the $B_1$ field strength.
This chapter does not account for these possible sources of error. It is also assumed that the \( B_1 \) mapping done with the off-resonant Bloch-Siegert shift pulse does not introduce any significant error when comparing it with the methods that use on resonant pulses. This is an accepted or overlooked assumption in all the publications using or referencing the BSS method. An evaluation of the accuracy of this assumption would be useful. However, it is not conducted here.

Chapter 3 briefly reviews the theory for each treated \( B_1 \) mapping technique. While these are developed in the provided references, a summary of the relevant equations was provided in chapter 3 for clarity and consistency of notation.

### 4.4 Methods

In this study, the theoretical probability density function (PDF) of the flip angle estimate is derived. Graphs are provided of each of the three methods for a range of SNRs. The calculated PDFs were verified with Monte Carlo simulation. Finally, actual repeated phantom measurements were performed at 3 T to verify both theory and simulation.

All experiments were performed on a Siemens (Erlangen, Germany) Tim Trio 3 T whole body scanner.

#### 4.4.1 Derivation of PDF of flip angle estimate

The PDF of the flip angle estimate for a given true flip angle provides complete information about the accuracy of the method. The true flip angle is unknown when using a technique to estimate flip angle. Therefore, the spacial variation is an unknown in practice so complete information about the accuracy of the method in practice is not possible. However, once the PDF has been determined, simpler useful measures of accuracy such as mean bias and variance of the flip angle estimate are also readily determined. To derive the PDF of the flip angle estimate for each \( B_1 \) mapping method, the noise corrupting the real and imaginary part of each image pixel value is assumed to be Gaussian white noise. Then the PDF of the flip angle estimate is derived based on the functional relationships unique to each method between the measured image pixel values and the flip angle.
4.4.2 Definition of System SNR and SNR efficiency

It is assumed that the equilibrium longitudinal magnetization, \( M_0 \), and the standard deviation, \( \sigma \), of noise for each \( B_1 \) mapping method are the same. Standard deviation of noise, \( \sigma \), is defined as the standard deviation of the real or imaginary part of each complex image pixel value (for a given voxel size, receive bandwidth, and total readout time). System SNR is defined as the ratio of these values, \( M_0/\sigma \).

Different \( B_1 \) mapping methods are optimally implemented with different sequence repetition times (TR), and therefore some methods are potentially faster than others. Methods with short repetition times might be conveniently implemented with a gradient recalled echo (GRE) acquisition with acquisition of one k-space line with each TR. Methods requiring longer repetition times may be more conveniently implemented with readout methods requiring fewer repetitions, such as echo-planar or spiral readout. An example of this approach would be the recent implementation of the Dual-Angle method with spiral readout by Cunningham et al. [37] for rapid-cardiac \( B_1 \) mapping. The interest is in comparing the accuracy of methods without regard to details of readout. To accomplish this while allowing each method to function at its optimal TR, the concept of signal-to-noise efficiency is incorporated in the analysis.

The signal-to-noise efficiency is proportional to the SNR and to the inverse of the square root of the imaging time. If one imaging method runs optimally with half the TR of another method, the faster method can acquire two signal acquisitions for every one acquisition of the slower method, thereby achieving a signal-to-noise efficiency advantage of a factor of \( \sqrt{2} \). This effect is accounted for in this analysis by scaling the SNR of the faster methods (i.e., the BSS method) by a factor equal to the square root of the number of signal averages they can perform for each single acquisition of the slower methods (e.g., the PS method). This approach correctly quantifies and compares the accuracy of each method operating at its optimal TR. This approach ignores the potential drawbacks of specific acquisition schemes (such as image distortion in an echo planar readout) and focuses instead only on the inherent accuracy of each method independent of specific readout methods.

However, the optimal TR for the BSS method cannot be generally specified. Under time constraints, the BSS method performs best by maximizing the max \( B_1 \) strength of
the BSS pulse subject to SAR constraints[36]. Without time constraints, the maximum $B_1$ allowed by a Siemens (Erlangen, Germany) TIM Trio SAR monitor for the specific setup described in the next section is determined. Using that $B_1$ value, the TR is minimized under SAR constraints and the idea of SNR efficiency is used to compare methods. Results are presented from the BSS method with various parameters determined empirically to present as fair a comparison as possible.

4.4.3 Practical SAR Limitations Experiment

As previously mentioned, the performance of the BSS method improves with increasing BSS-pulse power, but this is limited by SAR constraints. Work has been done to improve the performance of the method by investigating the tradeoffs between pulse length and SAR for various values of $T_2^*$[41]. In this analysis, a typical Fermi pulse envelope was used as published by Sacolick et al. [36]. Some improvement in performance may be possible with other RF pulse shapes.

To quantify the effect of SAR limits on achievable BSS-pulse energy in a realistic scenario, phantom experiments were performed where the BSS-pulse energy was varied to explore the SAR limits built into the scanner software [22]. For a given BSS pulse energy, the minimum sequence TR allowed by the scanner was determined. This experiment was performed twice with different RF coils: the built-in body coil, and a commercially available transmit-receive knee coil. Note that SAR constraints are dictated by many factors, including coil, anatomy being imaged, mass of sample being imaged, and method of calculation. Further work needs to be done in evaluating the SAR constraints of the BSS method, but is beyond the scope of this dissertation; a set of reasonable parameters was desired to allow validation of the analytical framework. Safe $B_1$ field strengths for the BSS pulse may be very different than those in these experiments, depending on implementation and application.

4.4.4 Parameter Choice

The parameters chosen for the theoretical PDF analysis were based on experimentally determined BSS SAR limitations and human tissue-like parameters at 3 T. Tissue parameters chosen were $T_1 = 1$ s and $T_2 = 40$ ms. Total scan time was assumed constant, and
parameters were then selected for each method to yield optimal accuracy and minimize noise in the allotted scan time. The PS and GRE-DA methods require a long TR for complete relaxation. The BSS method does not have the same requirement and is typically used in time constrained scenarios. However, as mentioned above, the $B_1$ strength will reach a peak value without time constraints, so multiple $B_1$ maps may be acquired and averaged in the same amount of time as a single $B_1$ map for PS or DA, resulting in an effectively higher SNR. Four BSS pulse strength/TR combinations were considered. The first combination corresponds to the parameters used in the phantom experiment for direct comparison to the experimental data. The remaining three combinations were based on the experiment to find practical SAR limitations described above: the second and third are based on data from the extremity coil, and the last on data from the body coil. An 8 ms Fermi pulse was used for the BSS pulse with a $K_{\text{BSS}} = 7401 \text{ rad/mT}^2$, similar to that published by Sacolick et al. [36]. The echo times were chosen to correspond to the phantom experiment, which employed the minimum TE allowed by the sequence for the given parameters. BSS parameters were: TR = 3 s, 91 ms, 651 ms, and 260 ms; TE = 13 ms; $B_{\text{1, nom}} = 10 \mu\text{T}, 4 \mu\text{T}, 11.5 \mu\text{T},$ and $24 \mu\text{T}; K_{\text{BSS}} = 7401 \text{ rad/mT}^2$. A longer echo time for the BSS method is a result of the 8 ms Fermi pulse and 1 ms gradient crushers before and after the BSS pulse. The Ernst angle was calculated and used as the nominal excitation angle. DA parameters were: TR = 3 s, TE = 3.84 ms, $\alpha_{\text{nom}} = 60^\circ$. PS parameters were: TR = 3 s, TE = 4.24 ms, $\alpha_{\text{nom}} = 90^\circ$.

**BSS Fermi Pulse:** The Fermi pulse envelope for the BSS has a form of

$$\frac{1}{\exp\left(\frac{(t-t_c)-m}{c}\right) + 1} \quad (4.1)$$

where $t$ is the time during the pulse, $t_c$ is the center time of the pulse, and $m$ and $c$ are parameters of the equation. The values used are $m = 2.769$ ms and $c = 0.17$ ms with a duration of 8 ms and $t_c$ of 4 ms. The envelope along with the spectrum is shown in figure 4.1. The frequency band containing 99% of the power assuming a Fourier transform relationship between the pulse and the power spectrum is 2.1 kHz. That means there will be negligible excitation with this pulse used at 4 kHz off-resonance.
4.4.5 Theoretical Model of Statistical Accuracy

Below the derivation for the BSS method PDF is presented. Following are the derivations of the PDFs for the PS and DA methods.

**Derivation of the PDF for the BSS $B_1$ Mapping Method:** The noise in each pixel of an MR image is modeled as a bivariate Gaussian distribution. Assuming a noise standard deviation $\sigma$ and a pixel magnitude $\rho$, the PDF of the phase $\Phi$ of that pixel is given by
Blackman[57]:

\[
\begin{align*}
    f_{\phi}(\phi) &= \frac{1}{2} \exp \left( -\frac{\rho^2}{2\sigma^2} \right) \\
    &\quad + \frac{\rho \cos(\phi - \phi_{BSS})}{2\sqrt{2\pi}\sigma^2} \exp \left( -\frac{\rho^2}{2\sigma^2} \sin^2(\phi - \phi_{BSS}) \right) \\
    &\quad \times \text{erfc} \left( -\frac{\rho}{\sqrt{2}\sigma^2} \cos(\phi - \phi_{BSS}) \right), \\
\end{align*}
\]

(4.2)

where \(\phi_{BSS}\) is the flip angle dependent phase resulting from the BSS pulse and \(\text{erfc}(x)\) is the complementary error function. The function \(\text{erfc}(x)\) is given by

\[
\text{erfc}(x) = \frac{2}{\sqrt{\pi}} \int_0^x \exp(u^2)du.
\]

(4.3)

The pixel magnitude \(\rho\) depends on factors such as sequence timing and relaxation times \(T_1\) and \(T_2\). This analysis uses a GRE sequence for the BSS method, resulting in a pixel magnitude given by the GRE signal equation

\[
\rho = \frac{M_0 \left( 1 - \exp \left( -\frac{TR}{T_1} \right) \right) \sin \alpha}{1 - \cos(\alpha) \exp \left( -\frac{TR}{T_1} \right)}.
\]

(4.4)

The phase difference of the two acquisitions for a given pixel is the random variable

\[
\Theta = \Phi^+ - \Phi^-,
\]

(4.5)

where \(\Phi^+\) and \(\Phi^-\) are the random variables representing the phase of the signal acquired after application of a BSS pulse with off-resonance frequency \(+\Delta\omega_{RF}\) and \(-\Delta\omega_{RF}\) respectively. The PDF of \(\Theta\), \(f_\Theta(\theta)\), is given by the convolution of the PDFs of the phase of each acquisition:

\[
f_\Theta(\theta) = \int_{-\pi}^{\pi} f_{\Phi^+}(\tau) \cdot f_{\Phi^-}(\theta - \tau) d\tau = f_{\Phi^+}(\theta) \ast f_{\Phi^-}(\theta).
\]

(4.6)

Solving equation 3.12 for \(B_{1,\text{peak}}\) results in

\[
B_{1,\text{peak}} \approx \left( \frac{\Theta}{2K_{BSS}} \right)^{\frac{1}{2}} = g(\Theta).
\]

(4.7)
The PDF of $B_{1,\text{peak}}$ can then be calculated by

$$f_{B_{1,\text{peak}}}(x) = \frac{f_\Theta(g^{-1}(x))}{|g'(g^{-1}(x))|}, \quad (4.8)$$

as described by Papoulis [58], where $g^{-1}(x)$ is the inverse of $g(\Theta)$ and $g'(\Theta) = dg(\Theta)/d\Theta$. The functions $g^{-1}(a)$ and $g'(\Theta)$ are then given by

$$g^{-1}(a) \approx 2a^2K_{\text{BSS}} \quad (4.9)$$

and

$$g'(\Theta) \approx \left(\frac{1}{8\Theta K_{\text{BSS}}}\right)^{\frac{1}{2}}, \quad (4.10)$$

which leads to

$$f_{B_{1,\text{peak}}}(x) \approx f_\Theta(2x^2K_{\text{BSS}})4xK_{\text{BSS}}. \quad (4.11)$$

Numerical methods were used to solve equation 4.11 (e.g., differences to approximate derivatives and interpolation to estimate function values at unavailable sample points as needed). Since the approximations used in equation 3.11 and equation 4.7 do not hold over the complete range simulated, Bloch simulations were used, which do not require those assumptions, to solve for the BSS signal level as well [21].

**Derivation of the PDF for the PS $B_1$ Mapping Method:** Analysis for the PS method parallels the BSS method. Equations equation 4.5 and equation 4.6 are equivalent to the BSS. Equation 4.8 from the BSS derivation becomes

$$f_\alpha(x) = \frac{f_\Theta(g^{-1}(x))}{|g'(g^{-1}(x))|}, \quad (4.12)$$
where

\[
f_\Phi(\phi) = \frac{1}{2} \exp \left( -\frac{\rho^2}{2\sigma^2} \right) + \frac{\rho \cos(\phi - \phi_{PS})}{2\sqrt{2\pi}\sigma^2} \exp \left( -\frac{\rho^2}{2\sigma^2} \sin^2(\phi - \phi_{PS}) \right) \times \text{erfc} \left( -\frac{\rho}{\sqrt{2}\sigma^2} \cos(\phi - \phi_{PS}) \right),
\]

(4.13)

instead of equation 4.2 and

\[
\alpha = g(\Theta),
\]

(4.14)

defining the function \( g \). The closed form solution to equation 4.14 is not straightforward so \( g^{-1}(x) \), and \( g'(g^{-1}(x)) \) were calculated numerically.

Equation 4.14 is based on the signal level (\( \rho \) and \( \phi_{PS} \)) with equations 3.6 - 3.8 providing the basis of the signal magnitude and phase with

\[
\rho = \sqrt{M_x^2 + M_y^2}
\]

(4.15)

and

\[
\phi_{PS} = \tan^{-1} \left( \frac{M_y}{M_x} \right).
\]

(4.16)

**Derivation of the PDF for the DA \( B_1 \) Mapping Method:** \( B_1 \) mapping with the DA method has a similar derivation to the BSS and PS methods. However, it is a magnitude-based method so equation 4.6 becomes

\[
f_M(m) = \frac{m}{\sigma^2} I_0 \left( \frac{m\rho}{\sigma^2} \right) \exp \left( -\frac{m^2 + \rho^2}{2\sigma^2} \right),
\]

(4.17)

where \( I_0(x) \) is a modified Bessel Function of the first kind expressed by

\[
I_0(x) = \frac{1}{2\pi} \int_0^{2\pi} \exp(x \cos \theta) \, d\theta.
\]

(4.18)
The PDF of equation 3.3 is
\[ f_t(r) = \int_{-\infty}^{\infty} |x| f_{m_1}(rx)f_{m_2}(x)dx, \] (4.19)
according to Papoulis et al.[58]. Equation 4.8 is used again with
\[ g(x) = \frac{1}{2\cos \alpha} \] (4.20)
to calculate the final PDF for the \( B_1 \) estimate of the DA method.

4.4.6 Monte Carlo Verification

Bloch equations were used for Monte Carlo verification of theoretical results. Signal was estimated using Bloch equations for each method. Complex Gaussian noise was added to the calculated signal levels. Noise magnitude was determined by the desired system SNR. Following the addition of noise, a \( B_1/\)flip angle estimate was calculated. The process was repeated 10,000 times per flip angle across a range of true flip angles, and PDFs, mean bias, and standard deviation of estimates were then calculated.

4.4.7 Experimental Verification

A 2% agarose phantom (by weight) was constructed and doped with 0.61 ± 0.01 mM CuSO\(_4\) with a \( T_1 \) of 890±40 ms and a \( T_2^* \) of 49±3 ms. \( T_1 \) and \( T_2^* \) measurements were verified immediately before all \( B_1 \) acquisitions. A planar phantom was used which measured 15 cm x 15 cm x 0.6 cm. The phantom size was chosen to produce a low system SNR, allowing the statistical model to be validated in a regime with more mean bias and larger standard deviation in a reasonable scan time. For all methods a TR of 5 s was used to eliminate any \( T_1 \) effects, matrix size of 512 x 64, 2D acquisition with a non-selective excitation, a 17 cm x 17 cm in plane field of view, and bandwidth of 400 Hz/pixel. For each method, 17 \( B_1 \) maps were acquired at 3 T. Echo times for each technique were as follows: BSS TE = 13.9 ms, DA TE = 3.84 ms, and PS TE = 4.24 ms. The phantom was imaged in the periphery of a commercial transmit-receive bird cage coil, where significant \( B_1 \) variation is present.
A truth dataset was constructed from the Dual-Angle method by averaging the 17 constituent images (increasing the effective SNR by a factor of $\sqrt{17}$) and creating a $B_1$ map from the averaged images. The $B_1$ map from the averaged images was then low-pass filtered for further reduction of noise. Data was used from the most uniform sections of the phantom, both in physical thickness and $B_0$ uniformity. The standard deviation and mean bias were then plotted as functions of the truth dataset.

The system SNR in the phantom experiment was calculated in order to correlate the experimental data with the theoretical results. The thermal equilibrium signal, $M_0$, for each pixel was estimated from the mean of the signal magnitude from the 17 images for each flip angle mapping method, based on the signal equation for each method and the transmit and receive coil sensitivities. Coil sensitivity at each pixel was based on the flip angle “truth” from a $B_1$ map formed with the DA method from the average of the 17 images. Measured $T_1$ and $T_2$ values of the phantom also figured into the calculation of $M_0$ according to the signal equation for each method. The standard deviation of noise was estimated from the real channel in the background of each method across the 17 images and over multiple pixel values. The standard deviation of the image noise for all methods was found to be identical within the expected error.

Both the analytical treatment and Monte Carlo simulations assumed a single system SNR across a range of flip angles. The experiment used a coil in an area of non-uniform receive sensitivity, so that system SNR varied with location. Therefore, the receive field is assumed proportional to the transmit field by the principle of reciprocity for direct comparison with experimental results.

The major focus of this experimental work is to validate the analytical framework for studying the performance of the various $B_1$ mapping methods. Such a validation does not require optimal choice of parameters, and the choice was made for the phantom experiment to normalize TR across each of the methods. Once the analytical framework is experimentally validated, it can be used to predict the performance of each method with any choice of parameters. New excitation schemes for the BSS method can be evaluated in this analytical framework as they become available.
Figure 4.2: Empirical measurement of TR constraints on BSS method due to SAR: minimum allowed TR as a function of BSS pulse amplitude determined empirically on the 3T scanner with different RF coils. Note that the extremity coil has more stringent constraints because its field is localized and likely less uniform than the body coil. The 16 ms BSS pulse used with the extremity coil has the same $B_1$,$\text{peak}$ as the 8 ms pulse, but twice the power.

4.5 Results

4.5.1 Practical SAR Limitations Experiment

Experimental results of minimum allowed TR for a given BSS pulse strength are shown in Figure 4.2 for three different cases. First, the blue trace uses an extremity bird cage coil with an 8 ms Fermi pulse used for the BSS pulse. Second, the green trace uses the same setup used in the first case except the BSS pulse is lengthened to 16 ms with unchanged amplitude, resulting in twice the BSS phase and twice the SAR. Finally, the red trace uses the body coil with an 8 ms Fermi pulse.

4.5.2 Theoretical Model of Statistical Accuracy

Figure 4.3 shows the theoretical PDFs for the Bloch-Siegert Shift method, GRE-Dual-Angle method, and the Phase-Sensitive method for different values of flip angle. For concise visualization of results, many one dimensional PDFs are displayed in a two dimensional picture: the horizontal axis represents the flip angle actually achieved; the vertical axis represents the PDF of the flip angle estimate; and the intensity is the measure of prob-
ability for estimation. Thus, each vertical line represents a PDF for a given true flip angle corresponding to the horizontal position on the line. Figures 4.4 and 4.5 show the mean bias and standard deviation, respectively, of the flip angle estimates at many actual flip angles.

A PDF with zero mean bias and zero standard deviation is a delta function at the theoretical flip angle. That PDF would appear as a diagonal line from the bottom left to the top right in figure 4.3. As standard deviation increases, the maximum value of the PDF decreases, which leads to a more broad and less distinct line (as is seen in the DA method). The BSS and PS methods have crisp lines except in areas of low-SNR. This indicates a low standard deviation of noise. Any curve in the PDF is a deviation from the ideal and represents a mean bias in the estimate. All methods show this deviation from the ideal at low flip angles in both standard deviation and mean bias.

Figures 4.4, 4.5, and 4.6 are simplified ways to display some of the information found in the PDFs. The axes on those figures represent $B_{1,\text{nom}}$ for the BSS method and $\alpha_{\text{nom}}$ for the PS and GRE-DA methods. $B_{1,\text{nom}}$ is related to the flip angle by a constant, $K_{EX}$, which depends on the excitation pulse being used. For example, a 1 ms hard pulse has a $K_{EX}$ of 268 rad/mT which translates into an $\alpha_{\text{nom}}$ of 122.8° for a $B_{1,\text{nom}}$ of 8 µT and an $\alpha_{\text{nom}}$ of 153.6° for a $B_{1,\text{nom}}$ of 10 µT. The greatest variation among methods is at low flip angle and low-SNR.

4.5.3 Monte Carlo Verification

Figure 4.7 shows the mean bias, standard deviation, and out of bounds measurements of the flip angle estimates at many actual flip angles comparing theory to Monte Carlo simulation. There is excellent agreement for all methods, giving confidence in the theoretical model. The only obvious deviation is in the DA method. As the actual flip angle of the DA method approaches 90° it becomes undefined.

4.5.4 Experimental Verification

Figure 4.8 shows the mean bias and the standard deviation results of the phantom experiment compared to theory. There is excellent agreement between the experimental results and theory. In the GRE-DA method the experimental data appears to diverge in
Figure 4.3: Theoretical probability distribution functions: Bloch-Siegert Shift method (left column), Phase-Sensitive method (center column), and Dual-Angle method (right column). System SNR of 10, 25, 50, and 100 from top to the bottom rows. Note that the PS and BSS method PDFs show up more clearly than the DA method because all PDFs are scaled the same and the DA method has a larger standard deviation which leads to a broader PDF. Each column in the image represents a probability distribution function at a specific flip angle or $B_1$ strength. The image intensity represents the value of the PDF for each possible flip angle (row). The nominal flip angles for the DA and PS method are 60° and 90°. The nominal field strength (which is proportional to flip angle) for the BSS method is 10 µT.
Figure 4.4: Analytical mean bias of flip angle estimate: Calculated at system SNRs of 10, 25, 50, and 100 (from top to bottom). Both axes are normalized by $\alpha_0$, the nominal flip angle for each method. Note that the Phase-Sensitive method performs consistently well and the Bloch-Siegert Shift method can perform well over a range of flip angles. However, the performance of the BSS method varies greatly with parameter choice. The choice of parameters for the BSS method are determined from SAR limitations caused by a homogenous body coil and likely not practical for cases with an inhomogenous $B_1$ field where a $B_1$ map is required.
Figure 4.5: Analytical standard deviation of flip angle estimate: Calculated at system SNRs of 10, 25, 50, and 100 (from top to bottom). Both axes are normalized by $\alpha_0$, the nominal flip angle for each method. Notice that all methods have increasing standard deviation of noise with decreasing flip angle and decreasing SNR. However, the phase-based methods (Bloch-Siegert Shift and Phase-Sensitive) can degrade slowly with careful parameter choice. This will lead to more accurate estimates of flip angle. The Bloch-Siegert Shift method has the best theoretical performance in low-SNR or low flip angle areas, but may be limited by SAR constraints.
Figure 4.6: Analytical out of bound measurements of flip angle estimates: Calculated at system SNRs of 10, 25, 50, 100 (from top to bottom). Both axes are normalized by $\alpha_0$, the nominal flip angle for each method. The Dual-Angle method flip angle estimates are undefined above actual flip angles of 90° ($1.5 \cdot \alpha_0$) or above. The probability of out of bounds measurements for the phase-based methods is significantly lower over a larger range of flip angles than for the DA method. The Phase-Sensitive method demonstrates a lower probability of out of bounds measurements than all other methods simulated with practical parameters at lower flip angles. The Bloch-Siegert shift method has consistently low probability of out of bounds measurements as the flip angles become greater.
mean bias from the analytical results. This is likely due to fewer data points being available at lower flip angles which causes the increase in mean bias to appear more steep as the density of data points in the horizontal direction decreases toward the left of the figure. A larger standard deviation of noise leads to a more broad clustering of experimental points around the theoretical line.

Figure 4.9 shows results from the phantom experiment. Mean flip angle/$B_1$ measurement appears similar for all methods due to the scaling of the images (top row). The standard deviation images (bottom row) have obvious differences between the different methods: the
Figure 4.8: Experimental results compared to analytic model: Plot of mean bias (top row) and standard deviation (bottom row) for the Dual-Angle method (first column), Phase-Sensitive method (second column), and Bloch-Siegert Shift method (third column) for the experimental results (blue dots) compared to the analytic model (black line). The system SNR, $T_1$, and $T_2$ were estimated to be 93, 900 ms, and 49 ms respectively. The experimental results and model are in very good agreement.

Dual-Angle method (left) demonstrated the highest standard deviation of measurement; the Bloch-Siegert shift method (middle) demonstrated a standard deviation of measurement lower than the Dual-Angle method but higher than the phase-sensitive method; while the phase-sensitive method (right) demonstrated the lowest standard deviation of measurement.

4.6 Discussion

The theoretical derivation of the PDF of the flip angle estimate for the BSS, DA, and PS methods of flip angle mapping is verified by both the Monte Carlo simulations and the experimental data from a phantom study. This analysis shows that the performance of the BSS method depends heavily on the power of the BSS pulse that is used, which is constrained
Figure 4.9: Mean and standard deviation from experimental validation: Mean of all phantom acquisitions is represented in the top row. Standard deviation of all phantom acquisitions is represented in the bottom row. Columns from left to right are the Dual-Angle method, the Bloch-Siegert shift method, and the phase-sensitive method. A surface coil was positioned at the bottom of the image. The signal drop-off is apparent as the distance from the coil increases in the phantom.

by SAR. SAR in turn depends heavily on the geometry of individual RF coils. When used at the SAR limits of the whole-body RF coil, the BSS method performs more accurately than either the DA or PS methods. For the smaller extremity coil, the PS method has the best performance not accounting for off-resonance effects. Including off-resonance in the analysis would potentially skew the mean bias or require additional time for a $B_0$ map, effectively lowering the SNR efficiency of the PS method. Sacolick et al. [36] stated that an optimal pulse shape maximizes the BSS without directly exciting spins in a sample. Interestingly, an optimal BSS pulse translates into optimal SNR efficiency of BSS $B_1$ mapping when TR is constrained by SAR. At times, image SNR efficiency increases with lowered flip angle and TR. However, when operating at the practical SAR limits of the scanner, a higher power
BSS pulse and corresponding longer sequence TR give better SNR efficiency than a lower power BSS pulse and shorter TR. The simulations suggest that this trend continues even to large values of TR; the accuracy of the BSS method is helped more by increased BSS pulse power at the cost of longer TR than by the possibility of signal averaging with shorter TR.

Use of the body coil for RF transmission allowed higher BSS pulse strength for a given TR than use of a less homogeneous extremity coil, giving better accuracy of flip angle measurement. However, measurement of flip angle is typically of most importance when coil sensitivity is inhomogeneous. Thus, the performance of the BSS method with the body RF coil may not be a realistic measure of the usefulness of this method in real world applications, where coil sensitivity inhomogeneity causes tighter SAR constraints which hurt the performance of the BSS method. In these situations the PS method is likely to give better accuracy, as was the case with the transmit-receive extremity volume coil.

A recent analysis of the PS and BSS methods [47] has suggested that the BSS method gives better accuracy than the PS method. As mentioned above in section 4.2, this analysis is limited by a choice of parameters which cripples the performance of the methods which typically require longer TR. For ease of implementation, the authors of that study chose the same TR (60 ms) for every $B_1$ mapping method they evaluated. This short TR resulted in SAR constraints which limited the PS method to a nominal flip angle of $35^\circ$ at 9.4 T rather than the typical nominal flip angle of $90^\circ$ that would be used with this method. Cunningham [37] published results of DA $B_1$ maps in vivo during a breath hold with longer TR. The TR of the PS method could be lengthened in a similar way. At this short TR and low flip angle, the performance of the PS method is severely compromised. The simulations have shown that for the $T_1$ of 1750 ms used in [47] the PS method achieves much higher SNR efficiency with a TR of 3000 ms, flip angle of $90^\circ$, and a single signal acquisition than with the parameters used by Pohmann et al. [47] at 9.4T (TR of 60 ms and flip angle of $35^\circ$) and fifty signal averages. This underscores the need when comparing flip angle mapping methods to operate each in the parameter regime where its SNR efficiency is optimized. The simulations confirm that the PS method gives best SNR efficiency when used with relatively long TR.

Interestingly, when using a constant off-resonance frequency the length or shape of the BSS RF waveform does not affect the tradeoff of SAR with $B_1$ estimation accuracy.
The phase created by the BSS pulse depends on the pulse energy, or the time integral of the squared RF pulse magnitude. SAR is represented by the same quantity. Therefore, any pulse with a given SAR has the same efficacy in creating BSS phase. One main consideration when designing the constant off-resonance frequency BSS pulse for a given $B_1$ mapping experiment is the maximum allowable SAR for the desired TR. Once the maximum allowable SAR is determined, the shortest and highest amplitude BSS pulse which creates this SAR can be designed. The shortest possible BSS pulse minimizes SNR loss due to $T_2^*$ signal decay. However, there is a tradeoff between the shortness of the BSS pulse and the sharpness of the transition band of the pulse’s frequency response, which is important for achieving the smallest off-resonance possible.

Monte Carlo simulations and experiment results shown in figures 4.7 and 4.8 demonstrate excellent agreement with the model which leads to a high level of confidence that the model is accurate. Having been validated by experiment, the model may be used to facilitate choice among $B_1$ mapping methods for specific cases.

Phantom construction for the experimental validation had many challenges:

- The $T_1$ had to be low enough for scan times that would allow the experiment to be conducted in a single session. There are a few references on matching phantom parameters to a desired value. However, most are applicable at lower field strengths and only provided general guidelines for matching parameters.

- The thin phantom required a container that was MR transparent. The low signal level allowed objects that typically were MR transparent to become visible like the silicone sealant used to seal the phantom.

- The edges of the phantom had to be tapered to minimize Gibbs ringing.

- The experiment setup could not include MR visible materials such as the sandbags typically used to position subjects or tape.

- Pressure caused the agarose gel MR properties to change. No pressure could be exerted on the gel.
• The gel had to be protected from drying during the experiment. The first version of the phantom included a venting hole to prevent condensation. Over the course of the experiment with that phantom, it had significant drying.

It was not obvious at the outset of the experiment endeavor that the phantom would cause such problems.

This analysis has focused on the SNR efficiency of $B_1$ mapping methods without regard to other specific details of pulse sequence design such as readout strategies. In practical implementation of a $B_1$ mapping sequence, other factors may be important. For instance, the BSS method lends itself to slice-selective $B_1$ mapping, while the PS and DA methods require non-selective excitation to avoid slice profile effects. This might make the BSS method advantageous for rapid single-slice $B_1$ mapping. The PS method has some sensitivity to $B_0$ inhomogeneity which may limit its performance in some environments. Implementation of echo-planar or spiral readout for rapid $B_1$ mapping with the PS or DA methods incurs increased complexity of pulse sequence design and image reconstruction, and may introduce image artifacts. In high-SNR environments, the noise performance of a method may be less important than its ease of implementation. It is likely for this reason that the DA method remains in widespread use despite its inferior noise performance. In any $B_1$ mapping application, the need for accuracy in the presence of noise must be balanced with practical considerations of implementation.

The PS method performs best in low-SNR environments. However, the applications for $B_1$ mapping can not be generalized into a single category of performance. Therefore, the right $B_1$ mapping method for different applications may be as varied as the applications.

4.7 Conclusion

In this work, a theoretical derivation of the statistical performance (probability distribution functions and derived mean bias, standard deviation, and probability of out of bounds measurements) is presented of the BSS, GRE-DA, and PS methods of $B_1$ mapping. The theoretical framework was validated with both Monte Carlo simulations and phantom experiments. All three showed excellent agreement. This statistical framework may be used to analyze the mean bias and standard deviation of flip angle estimates for any choice of
parameters for these methods. Many and varied applications exist such that no single $B_1$ mapping method can be recommended for all applications. However, an analysis like the one presented here will inform choice among $B_1$ mapping methods and can be tailored for specific applications.
Chapter 5

3D Selective $B_1$ Mapping

5.1 Introduction

Spatially selective excitation pulses are used to limit field of view and reduce scan time in 3D MRI [59, 60]. Variation in flip angle across the excitation volume will lead to variations in signal intensity. Signal intensity variations are undesirable for the varying contrast they produce [61] and they may lead to errors in quantitative measurements (e.g., measurements of $T_1$ [62, 63] or $T_2$ [64, 65]). Correcting these variations usually requires a knowledge of the flip angles or the $B_1$ field[62]. However, many $B_1$ mapping techniques fail in 3D slab-selective imaging because they operate on the assumption that flip angle scales linearly with transmit voltage at all spatial locations. For example, the Dual-Angle (DA) method [16, 56, 37] assumes that doubling the transmit voltage will double the flip angle in all voxels being mapped. This is a good assumption when non-selective excitation pulses are used, but this assumption breaks down near the edges of a selective excitation profile, potentially introducing large errors in flip angle estimates near the edges of the selected volume. $B_1$ mapping methods which do not depend on the assumption of linear scaling of flip angle with power such as the Bloch-Siegert shift [19] may not be effected by these spatial flip angle variations. The Actual Flip Angle Imaging (AFI) method relies on varying repetition time [17] and one implementation has been shown to be robust to selective excitation [66].

Methods that rely on this relationship between flip angle and transmit voltage are not limited to magnitude-based methods. Phase-based methods such as the Phase-Sensitive (PS) method [18] may also be effected. The original PS method was introduced with non-selective excitation and relies on a compound excitation pulse of $2\alpha_x \cdot \alpha_y$. The phase relationship generated by that compound excitation pulse can be mapped to flip angle by assuming there is always a 2:1 relationship between the flip angle achieved from each part of the pulse. If
it were modified for 3D slab-selective excitation, the flip angles across the imaging volume will not all have the same 2:1 assumed relationship across the entire volume imaged. This would lead to errors in flip angle estimates unless some correction were made.

Errors introduced by the assumption of a linear relationship between transmit voltage and flip angle are not constant in every situation and may vary with different sequence parameters including the RF pulse duration, RF pulse bandwidth, RF pulse shape [67], and the prescribed flip angle. The errors from this effect are minimal or non-existent at the center of the slab. However, at the edges of the 3D slab the errors are most pronounced. By understanding where the errors occur and the pulse sequence parameters that effect them, the errors may be mitigated and unreliable areas may be ignored or corrected. The goal of this chapter is to show that these errors are real and are significant in some cases. When using 3D slab-selective excitation for $B_1$ mapping, caution needs to be exercised in interpreting the results.

One example of 3D slab-selective excitation used in $B_1$ mapping is Wang et al. [68] who introduced a modification of the DA method which incorporates 3D slab-selective excitation to reduce the field of view. The potential error introduced by 3D slab-selection is recognized and the results are compared to 3D non-selective $B_1$ maps for verification. For the specific parameters and specific imaging scenario analyzed, Wang et al. found no significant errors, but there was no discussion on the limitation of the method due to potential error introduced from the 3D slab-selective excitation pulse. Caution needs to be exercised because errors introduced may be significant in some circumstances.

In this study, it is demonstrated that non-trivial errors may be introduced into $B_1$ mapping when using a 3D slab-selective excitation. This effect is demonstrated to be method specific through the use of Bloch simulations and experimental validation of these simulations for the DA and AFI methods. Through judicious choice/design of the RF pulse, $B_1$ mapping may be accomplished with a selective excitation. However, one must realize that $B_1$ estimates for many unmodified $B_1$ mapping methods may be invalid near the edges of a selectively excited volume.
5.2 Methods

5.2.1 Illustration of Error Introduced by 3D Slab-Selective Excitation

Errors are introduced into $B_1$ mapping when using 3D slab-selective excitation. These errors are easily demonstrated with a Bloch simulation of the Dual Angle (DA) method. Slab profiles are generated at two different flip angles ($60^\circ$ and $120^\circ$) using a Hamming windowed sinc for the RF pulse with a duration of 2 ms and a bandwidth of 7500 Hz. If the assumption of linear scaling of flip angle with voltage held true, the two profiles would be scaled versions of each other.

The differences between the two profiles are demonstrated by doubling the $60^\circ$ profile and overlaying the doubled profile on the $120^\circ$ slab profile as shown in figure 5.1(a). If the assumption of linearity between flip angle and voltage held, the doubled $60^\circ$ profile would be identical to the $120^\circ$ profile. There is an obvious deviation toward the edges of the profile.

True flip angles are known at each point in both slab profiles from the 3D magnetization output of the Bloch simulations. In a physical experiment, the true slab profile would not be known because of potential $B_1$ or $B_0$ inhomogeneities. All that would be known would be the DA estimate of the flip angle. This is shown in figure 5.1(b) with the DA method estimated slab profile overlaid with the simulated $60^\circ$ slab profile. Near the center of the slab, the estimate is accurate. However, the flip angle estimates quickly deviate from the true flip angles at the slab edges. In this case, the profile of the signal intensity would be consistent with the true slab profile and not the DA estimate. However, the differences between the DA estimated flip angle profile and the true flip angle profile could be more subtle than shown here and may not be obvious.

5.2.2 Definition of Normalized Slab Width

Before continuing, a definition needs to be made. The spatial extent of the slab profile (the slab width) is dependent on the bandwidth of the RF pulse and the strength of the selection gradient. This means that the slab width scales approximately linearly with the amplitude of the slab-selection gradient. If slab width is measured in physical distance,
Figure 5.1: Bloch simulation illustration of $B_1$/flip angle mapping error with a 3D slab-selective excitation pulse: (a) Achieved flip angles (solid lines) along with the expected profile if linearly scaling $B_1$ led to a linearly scaled flip angle. (b) Achieved flip angle (solid line) along with the Dual Angle Method estimate of the flip angle from the simulated data (dash-dot line).

then two different gradient strengths with the same RF pulse and other sequence timing held constant would have different slab profiles.

The errors introduced into $B_1$ mapping due to slab-profile effects do not depend on the strength of the slab-selection gradient. To render graphs independent of the gradient strength, the through-slab axis of all slab profiles are normalized by the prescribed slab thickness. This makes two slab profiles with identical RF pulses but two different gradient strengths, as mentioned above, identical. With slab profiles independent of the strength of the slab-selection gradient (just like the error is independent of the slab-selection gradient),
errors can be analyzed without worrying about the extra variable that would otherwise be involved.

5.2.3 Dual Angle Method

Phantom Experiment: An experiment was performed to validate simulation results that demonstrate the effects of a 3D slab-selective gradient on $B_1$ mapping. A uniform phantom was doped with gadolinium to shorten the $T_1$. With a shorter $T_1$, experiments could allow full relaxation of the magnetization in a reasonable amount of time. The phantom had $T_1/T_2^* = 40 \text{ ms}/35 \text{ ms}$. It was used to acquire 3D flip angle-maps using the DA method. A $B_1$ map was acquired using both a 3D slab-selective excitation and a non-selective excitation. The $B_1$ maps were acquired on a Siemens (Erlangen, Germany) TIM Trio 3T scanner with a Doty Scientific (Columbia, SC, USA) quadrature Litzcage coil and a custom built Transmit/Receive (TR) switch from Stark Contrast (Erlangen, Germany).

A Dual-Angle (DA) $B_1$ map was acquired using a Gradient Recalled Echo (GRE) sequence with a long enough TR to allow complete longitudinal recovery of the phantom. Two separate images were acquired at flip angles of $60^\circ$ and $120^\circ$. Imaging parameters were $\text{TR}/\text{TE} = 400 \text{ ms}/4 \text{ ms}$, matrix size $= 128 \times 64 \times 16$, a 3D slab-selective excitation, and a 3.84 ms readout.

Following the acquisition of a 3D slab-selective $B_1$ map, another DA $B_1$ map was acquired using a non-selective excitation and identical parameters except for a larger matrix size ($128 \times 64 \times 24$) to accommodate the entire phantom without aliasing.

Phantom Experiment True Flip Angles: Determining the true slab profile for the DA phantom experiment was challenging. Three options considered which do not accurately estimate the true slab profile are: (1) average DA method $B_1$ maps to increase the SNR; (2) use a non-selective excitation with the DA method; and (3) use the AFI method to measure the flip-angles. First, these methods will be explored and the reasons detailed of why they will not work. Then, the method used to determine the true slab-profile will be introduced.

A simple approach is to assume the errors correct themselves as the SNR improves. Averaging multiple acquisitions is a common way to improve SNR. If that were the problem,
the DA method could be used from images that were averaged to improve the SNR. Averaging does not work because the error is not due to a lack of SNR. The error is predicted in simulations of the DA method for slab-selective excitation when noise is not modeled.

Another option is using a non-selective excitation with the DA method. That will give the flip angles corresponding to the strength of the $B_1$ field across the phantom. To use the data from the non-selective DA $B_1$ map, the Bloch simulation which is being validated would have to be used to generate the true data. This becomes a partial circular argument. The simulation which is being validated would have to be used to validate the simulation.

Another option is to use the AFI method to measure the flip angles. The AFI method and DA method flip angle estimates do not match in the center of the slab. That difference needs to be reconciled for the AFI method to be used as the true flip angle for the DA method. The difference could be due to subtle differences in the pulse sequence implementations.

These methods are all inadequate for the purpose of validating simulations. Therefore, another way to accurately estimate the flip angle is needed. To estimate the achieved flip angle for the phantom experiments, three main ideas were used: (1) the DA method is accurate in the center of the slab; (2) the only variation in signal intensity is from flip angle because the phantom is uniform across the whole imaging volume and the coil used provides a nearly homogeneous $B_1$ field across it; and (3) the TR is long enough to allow complete relaxation. Complete relaxation allows the assumption of a simple signal equation of the form

$$\text{Signal}(x) = M \sin(\alpha(x)), \quad (5.1)$$

where Signal($x$) is the slab-position dependent signal, $\alpha(x)$ is the slab-position dependent flip angle, and $M$ is a constant that depends on many factors including proton density, $T_1$, $T_2$, and temperature. These ideas allow a true slab profile to be estimated without the problems of the previously mentioned three methods.

Equation 5.1 accounts for a flip angle which varies spatially but with a magnetization vector, $M$, that is constant with respect to location. The constant $M$ relates to the uniform phantom assumption.
The constant $M$ is unknown. It can be determined with the knowledge of the flip angle and signal intensity. The flip-angle estimate in the center of slab does not have errors from the slab-selective pulse. Consequently, the constant $M$ was determined in the center of the slab from the flip angle estimated using the DA method. The constant $M$ will be the same across the entire slab because the phantom is uniform. Finally, equation 5.1 was solved for $\alpha(x)$, the true flip angles for the phantom experiments.

The coil used was a custom designed volume coil with high SNR. Therefore, no significant errors were introduced into the true flip-angle estimate because of noise.

**Bloch Simulation:** The gradient strength, RF pulse shape, prescribed flip angle, phantom $T_1$ and $T_2$, and non-selective excitation maps were used to replicate the phantom experiment with a Bloch simulation for the DA method. The true flip angles for the DA method Bloch simulation experiments were known from the angle between the longitudinal axis and the simulated 3D magnetization vector.

**Phantom Experiment Compared to Simulation:** Figure 5.2 presents the results of these experiments for the DA method. The solid lines represent phantom data and the dashed lines represent simulated data. The black lines in figure 5.2 represent the true flip angles and the blue lines represent the flip angles estimated with the DA method in the standard fashion. Excellent agreement between the phantom experiment and simulation is demonstrated in both the truth flip angles and the DA method flip-angle estimates.

**5.2.4 Actual Flip Angle Imaging (AFI) Method**

**Phantom Experiment:** A phantom experiment was performed using the AFI $B_1$ mapping method with the same hardware and phantom as the DA experiment in section 5.2.3.

$B_1$ maps use an alternating steady-state spoiled GRE sequence for acquisition. One AFI $B_1$ map was acquired using a non-selective excitation and another with a 3D slab-selective excitation. Matrix size, readout duration, and TE were matched to the DA method parameters. The flip angle was 60° and $TR_1/TR_2 = 20$ ms/100 ms.
Figure 5.2: Validation of Bloch simulations with a phantom experiment for the DA method: Experiment results (solid) versus simulated results (dashed) showing both the true flip angles (black) and the standard DA estimate (blue).

There was no need for an alternate method to measure true flip angles for the AFI method since simulations demonstrate that the AFI method accurately estimates the flip angle.

**Bloch Simulation:** The gradient strength, RF pulse shape, prescribed flip angle, phantom $T_1$ and $T_2$, and non-selective excitation maps were used to replicate the phantom experiment with a Bloch simulation for the AFI method.

**Phantom Experiment Compared to Simulation:** Figure 5.3 displays the result of the phantom experiment and Bloch Simulation. Excellent agreement is shown between the phantom experiment and the Bloch Simulation.
5.3 Results

5.3.1 Illustration of Error Introduced by 3D Slab-Selective Excitation

Errors that may be introduced in the DA $B_1$ mapping method are demonstrated in figure 5.1. In figure 5.1(a) the error is demonstrated by comparing the expected slab profile from a $120^\circ$ flip angle with the actual $120^\circ$ slab profile. The expected $120^\circ$ slab profile is generated by doubling a $60^\circ$ slab profile. The actual $120^\circ$ flip angle profile is much more rounded at the edges as well as having a steeper fall-off. The nulls in both profiles occur at different locations. The sidelobes also demonstrate that the actual field profile can have sections of flip angle that are larger than expected as well as areas that are smaller than expected.

Figure 5.1(b) demonstrates the effect of the error demonstrated in figure 5.1(a) on the DA flip angle estimates. Instead of the expected decrease in flip angle at the edges of the slab, the DA estimate shows increasing flip angles. The estimated flip angles which increase

Figure 5.3: Validation of Bloch simulations with a phantom experiment for the AFI method: Estimated flip angles for the phantom (black) and simulation (blue) experiments.
are inconsistent with the decrease in signal in the constituent images from the $B_1$ mapping which would be observed in an experiment. The edges of the slab profile demonstrate the most obvious deviation in the flip angle. Even if these edges were ignored, there is still error throughout all but the very center of the slab. This error may be insignificant for a given situation.

5.3.2 Dual-Angle Method

**Phantom Experiment:** Again, as can be seen in figure 5.2 the phantom experiment results are shown by the solid lines: black for achieved flip angles and blue for estimated flip angles. The figure shows the DA estimate becomes invalid where flip angles are low. This is because the ratio of signal acquisitions is out of the range of the flip-angle estimating function.

**Bloch Simulation:** The Bloch simulation results are shown in figure 5.2 by the dashed lines. Similar to the phantom experiment, the gap in the flip-angle estimate is because the ratio of signal acquisitions is outside the range of the flip angle estimating function.

**Simulation Validation in a Phantom:** Excellent agreement between simulation and phantom experiment is shown in figure 5.2 for the DA method. The estimated achieved flip angle profile from the phantom experiment is in excellent agreement with the achieved flip angle in the Bloch simulation. Likewise, the flip angles estimated with the DA method also show excellent agreement. Accordingly, these results lend credibility to the simulations performed. The phantom experiment DA method estimates flip angle in some areas where the simulation cannot estimate flip angle. Moreover, this is likely due to noise which is present in the phantom scan causing the ratio of signal acquisitions to fall within the range of the flip angle estimating function.

5.3.3 Actual Flip-Angle Imaging method

**Phantom Experiment:** As has been noted earlier, the phantom experiment results are shown in figure 5.3 by the black line. Here, gaps in the flip-angle estimate are due to the ratio of signals used being outside the range of the flip angle estimating function. Significantly,
the deviation on the right side is not visible in the constituent images and is likely due to low SNR and the sensitivity of the estimating function. Nonetheless, the profile is the general expected shape.

**Bloch Simulation:** Similarly, the Bloch simulation results are also shown in figure 5.3 by the blue line. Again, as noted in the phantom experiment results above, gaps in the profile are due to the signal ratios being outside the flip angle estimating functions range. In spite of the gaps in the profile, it is the general expected shape.

**Simulation Validation in a Phantom:** The AFI method experimental results show excellent agreement with the Bloch simulations in figure 5.3. There is a small deviation between the absolute values estimated in the center of the profile and to one side. However, the general shape and magnitude of the profile are in agreement. Here, the AFI estimated flip angles are only shown since the method of estimating the true flip angles for the DA method is not valid with this method. Simulations show that the AFI method is accurate in estimating the flip angle. As mentioned earlier, the minor deviation between the phantom experiment and Bloch simulation in the last point on the right side is likely an effect from low SNR in the phantom experiment. The agreement between the Bloch simulation and experimental results lends credibility to the conclusion that the AFI method accurately estimates the flip angle even with 3D slab-selective excitation in use.

### 5.4 Discussion

The errors introduced into $B_1$ mapping by a 3D slab-selective excitation should be a consideration every time slab-selective excitation is used with $B_1$ mapping. Certain situations may be able to tolerate the error introduced. However, these errors may be severe as shown in figure 5.1. Therefore, these effects should be considered.

Typically, the edges of the slab profile are ignored in imaging. This is where the worst of the errors are introduced. However, if the error prone areas are not phase encoded, they will wrap into the desired field-of-view. The errors introduced from the slab edges aliasing into the field of view are beyond the scope of this chapter. The purpose of this chapter is to demonstrate that errors introduced into $B_1$ mapping by 3D slab-selective excitation
can be a significant issue and need to be considered when $B_1$ mapping is performed with a slab-selective excitation.

In like manner, slice-selective excitation for 2D imaging also has negative effects on $B_1$ mapping if not accounted for. Furthermore, the analysis for 2D slice-selective excitation is similar to that shown here for 3D slab-selective excitation. In fact, it was previously analyzed by Bouhrara and Bonny [20].

Figure 5.2 demonstrates that the errors predicted by Bloch simulation are verifiable in a phantom and that the DA method may have significant errors introduced by 3D slab-selective excitation. This lends credibility to the argument that these errors occur in vivo. The blue lines which represent the typical flip angle estimate with the DA method have unexpected deviations from the expected slab-profile. The expected slab-profile is shown by the estimated true flip angles in the solid lines. The DA method estimate deviates significantly from the expected slab-profile near the edges and cannot be relied on without correction for a $B_1$ estimate.

Figure 5.3 demonstrates that the AFI method simulations are validated by the phantom experiment. True to its name, the AFI method estimates the actual flip angle.

Chapter 6 introduces a method to correct the error and some metrics to quantify the error involved. This error correction may allow a broader range of $B_1$ mapping methods to be used with selective excitation.

The methods in this chapter may be applied to other situations or $B_1$ mapping methods to predict the level of error expected in an experiment. This will help identify the slices in the slab which will have unacceptable results and ignore those areas in post-processing.

5.5 Conclusion

As can be seen, this chapter demonstrates that significant error can be introduced into $B_1$ mapping through the use of 3D slab-selective excitation using Bloch simulations. Furthermore, phantom experiments are used to verify Bloch simulation results for the DA $B_1$ mapping method and the AFI $B_1$ mapping method. However, the DA method is demonstrated to have error introduced from 3D slab-selective excitation whereas the AFI method performs well with 3D slab-selective excitation. Accordingly, the effect is method dependent.
Ultimately, further work needs to be done in quantifying the $B_1$ error introduced by slab-selective $B_1$ mapping. Chapter 6 introduces some simple metrics to aid in that work. It also demonstrates a method of correction for cases that require a 3D slab-selective excitation with a $B_1$ map. However, one may still avoid the errors identified in this chapter if caution is used during all $B_1$ mapping. The methods outlined in this chapter can be duplicated for other situations or $B_1$ mapping techniques to inform experiment design.
Chapter 6

Measuring and Correcting Errors Introduced by 3D Selective $B_1$ Mapping

6.1 Introduction

Signal intensity variation in an MRI image as a result of RF field inhomogeneity leads to errors in quantitative measurements [62, 63, 64, 65] and variations in contrast [61] which can lead to errors in interpreting the image. Often, 3D slab selective excitations may be used to limit the field-of-view and decrease scan time [59, 60]. In chapter 5, it was demonstrated that errors appear in some $B_1$ mapping techniques when a 3D slab-selective excitation is used. In this chapter, a method for using Bloch simulations to correct errors introduced from slab-selective excitation is presented. Additionally, metrics for measuring that error are proposed and used to further evaluate what parameters are most influential on the error. The methods presented in this chapter, when applied, will increase the accuracy of $B_1$ mapping, improve quantitative measures relying on $B_1$ mapping, and potentially improve the diagnosis and study of diseases.

The general method for correcting errors introduced through 3D slab-selective excitation uses Bloch simulations to predict the error and then correct for it. The Bloch simulations are used to estimate the signal that a given RF pulse shape and gradient will produce for each slab and at a range of flip angles. Then, that signal is used as a look-up-table (LUT) to determine the $B_1$ or flip angle.

The RF pulse used for slab-selective excitation has a dramatic effect on the errors introduced in $B_1$ mapping. The metrics are used to evaluate the effect of RF pulse duration, RF bandwidth, and flip angle on the errors introduced by the 3D slab-selective pulse used for $B_1$ mapping.
An example of 3D slab-selective $B_1$ mapping shows how the presented method is effective with the Dual Angle method [16, 56, 37].

6.2 Methods

6.2.1 Correcting Errors in $B_1$ Mapping Caused by 3D Slab-Selective Excitation

The error correction method was validated with phantom tests. First, data was acquired that exhibits errors caused by 3D slab-selective excitation. In addition, a data set with identical parameters was acquired with a non-selective excitation pulse in order to validate the correction method. For the phantom experiment, a uniform fluid phantom doped with gadolinium ($T_1/T_2^* = 40$ ms/35 ms) was used. Four data sets were acquired: two with a 3D slab-selective gradient recalled echo (GRE) pulse sequence and two without. Both the 3D slab-selective excitation set and the non-selective excitation set had identical parameters except for the type of excitation and matrix size. Matrix size for the non-selective excitation was larger (128 x 64 x 24) to avoid aliasing due to the larger excitation area. Flip angles were $60^\circ$ and $120^\circ$. A sinc shaped RF pulse was used for selective excitation and a hard pulse was used for non-selective excitation. Imaging parameters were TR/TE = 400 ms/4 ms, matrix size = 128 x 64 x 16, and a readout of 3.84 ms. The images were acquired on a Siemens (Erlangen, Germany) TIM Trio 3T scanner with a Doty Scientific (Columbia, SC, USA) quadrature Litzcage coil and a custom built Transmit/Receive (TR) switch from Stark Contrast (Erlangen, Germany).

Bloch simulations were used with a priori details specific to the pulse sequence to generate a look-up-table (LUT). The LUT was used to estimate the actual flip angles and $B_1$ from the acquired data. Presently, the focus is on the Dual Angle (DA) method of $B_1$ mapping. However, the method is general and may be applied to any $B_1$ mapping method that can be accurately simulated with a Bloch simulation.

6.2.2 Measurement of Error

Error will be measured as the percent difference between the estimated flip angle and the "true" flip angle as defined in chapter 5. Three figures of merit will be used to compare the error in different scenarios. Two figures of merit refer to the error: maximum error within
the prescribed slab width and width of the center section where the error is below a specified threshold. The third metric is related but not a direct measure of error. It is the extent of sampling required in the slab select direction to avoid aliasing. In this analysis we have not considered the errors introduced by aliasing which comes from insufficient sampling in the slab direction. Therefore, it is important to understand the extent of sampling required to avoid aliasing. All three figures of merit are discussed in more detail below.

**Maximum Error:** The maximum error is calculated from within the prescribed slab thickness. The prescribed slab thickness was chosen to correspond with the full-width half-maximum bandwidth of the RF pulse. Often data is acquired from outside the visualized slab thickness to reduce aliasing; however, it is usually ignored. Therefore, even though the error will likely be worse outside of the prescribed slab thickness, it would not be meaningful to measure the error beyond that.

**Confidence Width:** The confidence width is the extent of the slab profile where there is confidence in the $B_1$ estimate. It is measured as the width of the slab profile that has error below a threshold. It is reported as a percent relative to the prescribed slab thickness. The threshold needs to be defined for every quoted confidence bandwidth. It is measured relative to the bandwidth of the RF pulse. For example, suppose a 3% error can be tolerated. If the error is less than 3% across 75% of the prescribed slab thickness, then the confidence width is 75%.

**Sampling Extent:** The required sampling extent is based on a signal level threshold. Everywhere the signal is above the threshold needs to be phase encoded to avoid aliasing above the threshold. This is reported relative to the bandwidth of the RF pulse.

### 6.2.3 Sequence Parameter Effects on Error

The effects of 3 parameters on the error introduced by slab-selective excitation were evaluated: RF pulse bandwidth, RF pulse duration, and prescribed flip angle. Actual flip angle variations across the slab ("true" flip angles) and signal intensities were calculated directly with Bloch simulations that do not rely on the small tip angle approximation. Typi-
cally, $B_1$ mapping methods require two acquisitions with one or more parameters changed to negate effects not of interest. Bloch simulations were repeated as required for each method. This yielded two sets of simulated signals. The ratio of the signals is used for the input of the LUT. The achieved flip angles in the Bloch simulations are known and used as the outputs of the LUT. The LUT is then used to estimate the flip angle variations across the slab. Here we detail the Dual Angle $B_1$ mapping method. However, the process is general and could be repeated for any method that can be represented with Bloch simulations.

For each parameter evaluated, a new simulation is performed at a range of different values for that parameter. The figures of merit were measured and the results are reported. There is a separate set of graphs for each parameter evaluated and each figure of merit. The independent axis of each graph is the parameter being evaluated. The dependent axis is the figure of merit being measured.

6.3 Results

6.3.1 Effect of 3D Slab-Selective $B_1$ Mapping

Figure 6.1 shows the results from the DA $B_1$ mapping method with correction for 3D slab-selective excitation. Data shown includes the truth flip angle and truth $B_1$ map and the DA flip angle map and $B_1$ map with correction for 3D slab-selective excitation. The truth flip angle map and the DA flip angle map with corrections match very well. The truth $B_1$ map and DA $B_1$ map with corrections also correlate well. The truth flip angle and $B_1$ maps required two different experiments. The DA flip angle map and $B_1$ map were calculated from a single data set. The DA corrections are only valid over a limited range because the LUT only has a limited section where it is monotonically increasing.

6.3.2 Sequence Parameter Effects on Error

RF pulse bandwidth is the first sequence parameter evaluated with the introduced metrics. Figure 6.2 shows the confidence bandwidth (top), maximum error (middle), and sampling extent (bottom). The confidence bandwidth increases as RF pulse bandwidth is increased. The maximum error also increases as the RF pulse bandwidth increases. The sampling extent decreases as the RF pulse bandwidth increases.
Figure 6.1: DA $B_1$ map with corrections for 3D slab-selective excitation: Two scenarios are represented here. First, the dashed and dot-dash lines represent the distribution of $B_1$ power across the slab. The dot-dash line is a DA $B_1$ map without slab-selective excitation. The dashed line is generated from the DA method with a 3D slab-selective excitation and represents the flip angle that would be achieved in the center of the slab with the same $B_1$ power. The solid and dotted lines are the flip angles achieved with 3D slab-selective excitation. The solid line is the estimated truth from the phantom experiment as described in the text. The dotted line is the flip angle estimated with the Dual Angle method accounting for 3D slab-selection.

Next, a related parameter is evaluated: RF pulse duration. Figure 6.3 shows the confidence bandwidth (top), maximum error (middle), and sampling extent (bottom). The confidence bandwidth increases as RF pulse duration is increased. However, the transition is not smooth. The maximum error increases in a smooth manner as the RF pulse duration increases. The sampling extent decreases as the RF pulse duration increases.

Last, the flip angle is evaluated with the introduced metrics. Figure 6.4 shows the confidence bandwidth (top), maximum error (middle), and sampling extent (bottom). The confidence bandwidth increases as flip angle is increased. However, the increase is concave
and not convex like the other parameters. The maximum error increases concavely with flip angle. The sampling extent increases as the flip angle increases.

6.4 Discussion

6.4.1 Effect of 3D Slab-Selective $B_1$ Mapping

The effect of 3D slab-selection breaks down the typical assumption that a doubling of RF power doubles the flip angle. This leads to a breakdown between assuming $B_1$ mapping and flip angle mapping are equivalent. Figure 6.1 demonstrates this by showing a flip angle profile equivalent to a $B_1$ profile (dashed and dash-dot lines) along with the flip angle profile
achieved (solid and dotted lines). The reference lines (dash-dot and solid) were created with a non-selective dual angle map for the $B_1$ type profile (dot-dash line) and the assumption of a uniform phantom for the actual flip-angle profile (solid line). The dashed and dotted lines are from the phantom experiment data corrected with a LUT created from Bloch simulations. Both profiles (dashed and dotted lines) were estimated from the same experiment with LUTs generated from the same Bloch simulations. Therefore, not only can errors be corrected in the DA method when slab-selection is present, the $B_1$ profile and flip angle profile can be estimated simultaneously.
6.4.2 Sequence Parameter Effects on Error

Increasing the RF pulse bandwidth, RF pulse duration, or flip angle increases the confidence bandwidth and maximum error. The characteristics of the different curves show differences. The RF pulse characteristics are related and increase rapidly in the lower range of parameters and more slowly at the higher range of parameters. The flip angle curves increase slowly at low flip angles and more quickly at the mid- to high- range values.

An increase of the confidence bandwidth and the maximum error simultaneously indicate a sharper edge to the slab profile with a more narrow transition. The higher confidence bandwidth is better for $B_1$ mapping as long as the error zones are avoided. The sharper edge
to the slab profile also supports the decreasing sampling extent required as the RF pulse bandwidth and duration are increased.

Even though the confidence bandwidth and the maximum error are increasing with flip angle, the maximum signal is also increasing. This explains the increasing sampling extent. Since the threshold is a fixed signal level, as the signal level increases everywhere the point where the threshold is crossed is going to expand.

6.5 Conclusion

A general method for correcting the errors in 3D slab-selective $B_1$ mapping is introduced and applied to the DA method as an example. The results are very promising with how well the corrected $B_1$ map matches the expected results. In addition, both the $B_1$ profile and flip angle profile—which are different in the presence of slab-selective excitation–can be estimated simultaneously.

As has been noted previously, metrics are also introduced to quantify the error and sampling required for 3D slab-selective $B_1$ mapping. The metrics were then used for an analysis of the error on the DA method. The analysis shows that increasing RF pulse bandwidth or duration is beneficial for $B_1$ mapping when 3D slab-selective excitation is used because that increases the confidence bandwidth.
Chapter 7

Other Contributions

7.1 Decoupled RF-Pulse Phase-Sensitive $B_1$ Mapping

7.1.1 Introduction

$B_1$ mapping is an important component of quantitative MRI and parallel transmission [18, 36]. Analyses by Morrell and Schabel [28], Allen et al. [25], Pohmann et al. [47], and Park et al. [23] have begun to shed light on the strengths and weaknesses of many of the $B_1$ mapping methods. However, there is still no clear method that is superior. Phase-based $B_1$ mapping methods have shown great potential with consistency while measuring large ranges of flip angles, especially in lower SNR environments. One of the phase-based methods, the Bloch-Siegert Shift (BSS) method, has demonstrated potential for characterizing parallel transmission systems because of the ability to separate excitation from the $B_1$ encoding pulse. This allows for a more homogeneous excitation pulse to maximize the MR signal followed by the $B_1$ encoding pulse (e.g., parallel transmit array or body coil excitation and individual coil $B_1$ mapping).

In this section, a modification of Morrell’s Phase Sensitive (PS) $B_1$ mapping method is introduced which allows separation of the $B_1$ encoding from the excitation pulse for greater flexibility while still achieving accurate $B_1$ mapping. It will be referred to as the Decoupled RF-Pulse Phase Sensitive (DPPS) method. The DPPS method also allows the flip angle mapping to be tailored to the desired range of flip angles. Following the description of the new technique, a brief statistical analysis of the DPPS method’s performance (mean bias and standard deviation of flip angle estimate) relative to other $B_1$ mapping techniques using Monte Carlo simulations is demonstrated. The statistical analysis suggests that the DPPS method achieves excellent performance in low SNR scenarios.
7.1.2 Theory

The Phase Sensitive method typically uses a compound excitation pulse of \(2\alpha_x - \alpha_y\) from the same RF source. This new method decouples the compound excitation pulse found in the PS method which allows more freedom to tailor \(B_1\) mapping for specific needs. This decoupled pulse is \(\beta_x - \alpha_y\), where \(\beta_x\) is effectively the \(B_1\) encoding pulse and \(\alpha_y\) can be considered the excitation pulse. The pulse sequence diagram is shown in figure 7.1. The first RF pulse, \(\beta_x\), rotates the initial magnetization in the \(yz\)-plane as depicted in figure 7.2(a). While figure 7.2(b) depicts the second RF pulse, \(\alpha_y\), that rotates any magnetization in the \(yz\)-plane into the \(xy\)-plane for readout. The two RF pulses do not need to come from the same coil. However, if two different coils are used they must generate fields that are perpendicular to each other.

7.1.3 Methods

**Simulations:** Monte Carlo simulations were run using 1000 realizations on the DPPS method along with three other methods: Dual Angle (DA), Phase Sensitive, and Bloch-Siegert Shift. The assumed system SNR, as defined in [23], is 200. TR is assumed infinitely long, TE=0 ms, and differences in imaging time are not accounted for. Axes are scaled relative to the nominal flip angle for each method. The nominal flip angles are 60° (DA) and 90° (DPPS and PS) with the nominal \(B_1\) for the BSS method is 0.1G. All methods use gradient echoes. BSS parameters: \(K_{BSS} = 74.01 \text{ rad/G2}, \alpha = 90^\circ\). For the proposed method \(\alpha_y\) is a constant 90° while \(\beta_x\) varies. A second RF source with uniform field is assumed available for the proposed method and the BSS method. Results are shown in figure 7.3.

**Hardware for testing:** So far, the validation of this method has only been performed theoretically in simulations. Parallel transmit hardware is not common on MRI machines because it is experimental. One type of MRI machine which typically has parallel transmit hardware installed is on high-field (7 Tesla) MRI machines. All high-field MRI machines are experimental. The University of Oxford has one of these machines. Through collaboration
Figure 7.1: Decoupled-pulse phase-sensitive $B_1$ mapping method pulse sequence diagram: The decoupled-pulse phase-sensitive (DPPS) $B_1$ mapping method has many similarities with the original PS method. However, the DPPS method is more flexible by allowing the different components ($\beta_x$ and $\alpha_y$) of the compound-excitation pulse to vary independently rather than fixing the $\beta_x/\alpha_y$ ratio to 2. This allows the method to be extended to parallel transmit MRI. The gradients depicted represent a Cartesian readout scheme. However, the method is not limited to a Cartesian readout scheme and may benefit in acquisition time from a center-out trajectory.

with them, the author is constructing a parallel transmit MRI coil. The desire is to validate the method on that system in the near future.

The design for the parallel transmit coil under construction is based on transmission line elements arranged in an array as introduced by Adriany et al. in 2005 [69]. More recently, a similar design has been used for cardiac imaging [70]. In 2012, Snyder et al. compared a 16 element array to an 8 element array concluding that the 16 element array produced an increase of 22% in SNR over the 8 element array. However, it was noted that the 16 element array was considerably more complex to construct and optimize [71]. The
Figure 7.2: Decoupled-pulse phase-sensitive method magnetization evolution: This figure demonstrates the effect of both decoupled RF components from the pulse sequence. Part (a) depicts the $\beta_x$ pulse rotating the magnetization in the yz-plane followed by the $\alpha_y$ pulse depicted in part (b) rotating any magnetization in the yz-plane into the xy-plane for readout.

Figure 7.3: Mean bias and standard deviation of DPPS $B_1$ mapping method compared to other methods: (top) mean bias of the DPPS, DA, PS, and BSS methods of $B_1$ mapping with (bottom) standard deviation of the same at a system SNR of 200.
University of Oxford system is only equipped with 8 channels, so the decision was made to base the coil design on the 8-channel 2012 design of Snyder et al.

The coil construction is almost complete for half of the 8 element array. The design used is smaller than that used by Adriany et al. to better match the targeted anatomy (the hip). The largest remaining factor is tuning and decoupling the coil. This is best performed at the University of Oxford where the coil can be tested. Therefore, that process is waiting for another trip to the University of Oxford by the author. Pictures of the coil in its current state are displayed in figure 7.4(a).

7.1.4 Results and Discussion

The mean bias and standard deviation for the DPPS method are nearly zero in the case where a uniform excitation field is available apart from the field to be mapped. The uniform mean bias and standard deviation are a result of a uniform signal magnitude in the resulting image from tipping the yz-plane completely into the xy-plane. The DPPS method of flip angle mapping achieves great accuracy in situations where the sensitivity of one element of an array is being mapped. Please note, two coils used to map the $B_1$ field this way must generate fields that are orthogonal to each other. The current results were obtained for flip angles ranging from zero to $2\pi$. In practice, any range of flip angles including angles greater than $2\pi$ can be measured by this method if phase images are correctly unwrapped.

7.2 Ultra-Short TE (UTE) Imaging of Brain Lesions

Some tissues have $T_2$ values which are too short to be seen in conventional clinical imaging [72]. A general class of techniques that attempts to image those short $T_2$ tissues is call Ultra-Short TE (UTE) MRI. One common approach to UTE imaging is to use a center-out sampling scheme rather than the standard Cartesian line-scanning technique. Standard Cartesian line-scanning techniques require time before the echo for image encoding. Initial UTE imaging at Brigham Young University has used a 3D Cones [73] center-out trajectory. This method uses the MRI hardware at its limits in order to improve the sampling sampling efficiency. Improved sampling efficiency means less time is required for imaging.
(a) Inside pTx coil case showing 4 channels  

(b) Closed coil housing for pTx coil

Figure 7.4: Half of the 8 channel pTx MRI coil in construction for Oxford: Current state of the coil being made in collaboration with the University of Oxford. (a) Shows an inside view of the coil housing which exposes the 4 elements and associated hardware. (b) Shows the outside of the coil housing and associated cables for transmit and receive connections.

It is not sufficient to shorten the echo time to achieve good results with UTE imaging. Even with an ultra-short echo time, the signal from short $T_2$ components will be obscured by signal from the long $T_2$ components. To counteract this effect, UTE imaging relies on two image acquisitions at different echo times. The first echo time is as short as possible, 1 ms or less. The second echo time is a couple milliseconds later, depending on the desired contrast. The difference of those two echo times is what constitutes the UTE image. The general concept is that long $T_2$ species will not have much decay over the time between
echoes. Therefore, the difference image will negate all the strong signal coming from long $T_2$ species allowing the short $T_2$ species to be visible with high contrast.

UTE imaging is typically used for objects with extremely short $T_2$, on the order of 1 ms. Short $T_2$ objects are usually more solid like bone and tendon in the body. Rubber is a material that is more solid and has short $T_2$. Rubber does not typically appear on MR images. In figure 7.5(c), the rubber bands show up as signal voids. Therefore, rubber bands were used for some initial testing of the UTE sequence. Those results are in figure 7.5.

One of application of UTE imaging I assisted with was an attempt to image brain lesions in a cadaveric specimen from a subject with Alzheimer’s. The disease is characterized by a build up of protein lesions in the brain. Protein has a short $T_2$, so the goal is to highlight these lesions with UTE imaging. Results are not yet validated with this project. However, the initial images (an example is found in figure 7.6) are promising because the UTE imaging does show potential lesions[27]. The next step is to correlate those images with histology to validate the hypothesis. If validated, the study of Alzheimer’s disease could be accelerated through study of the plaques; by watching the development of Alzheimer’s plaques in vivo.
Figure 7.6: UTE image of excised Alzheimer’s brain: (a) An ultra-short echo time image of an excised brain from a person who had Alzheimer’s along with the (b) short and (c) long echo time images used to generate it. Note the enhancement in the UTE image that is not present in either of the other images. This indicates there may be an Alzheimer’s plaque at that point.

and studying the plaques ex vivo. This could lead to earlier diagnosis, better treatments, and possibly a cure for Alzheimer’s.

My contributions to this project are a result of being integrally involved in UTE imaging at BYU. My pulse sequence development expertise along with work I have done with non-Cartesian imaging and reconstruction has been the foundation for UTE imaging. The UTE pulse sequence has been maintained by me since I started at BYU.

7.3 Diffusion Tensor Imaging with the qDESS Technique

The qDESS MRI pulse sequence is a promising new technique that allows the measurement of diffusion and $T_2$ along with good morphology in a fast steady-state sequence. Recently this was shown by Staroswiecki et al. [74].

The goal of this project was to utilize the ADC measurements at different angles to produce diffusion tensors. This allows determining not only the magnitude of the diffusion in one direction but determining the direction of greatest diffusion and the anisotropy of the diffusion. Strong directional diffusion often indicates some biological process of interest such as connections in the brain.
The biological process of interest to me is the collagen structure of cartilage. With osteoarthritis, the collagen structure of cartilage degrades. The hypothesis is that the collagen degradation could be visualized before current MRI techniques allow. A more sensitive measure of cartilage damage could allow more cost effective studies of the disease, earlier diagnosis, better treatments, and better patient outcomes.

My contribution to this project was some of the initial thinking along with programming of the pulse sequence to perform these measurements and some initial work on the reconstruction.

7.4 Phase-Sensitive Sodium \( B_1 \) Mapping

Sodium imaging with MRI is inherently low SNR. Due to the characteristics of the sodium nucleus and the low abundance in the body compared to hydrogen, sodium generates less than 5% of the signal that hydrogen does in the body. \( B_1 \) methods are usually developed in relatively high SNR environments compared to sodium. The phase-sensitive \( B_1 \) mapping method was the first to succeed in accurately mapping the \( B_1 \) field for sodium.

This project was one of my first and created a strong foundation for my BSS analysis. My major contribution in this project was pulse sequence support for the sodium imaging component. As mentioned previously I have had charge of the 3D cones sequence, trajectory generation, and reconstruction at BYU. Initially we started using 3D cones so we could image sodium better.

7.5 Performance Comparison of a Hybrid Dual-Tuned \(^{23}\text{Na}/^{1}\text{H} \) Birdcage to a Single-Tuned \(^{23}\text{Na} \) Birdcage with Identical Geometry

As mentioned in the previous section, MR imaging in sodium produces a much lower SNR than hydrogen. Much lower SNR leads to much larger voxel sizes. Much larger voxel sizes mean structures are more difficult to identify. One method for realizing structural information is to perform standard hydrogen MRI in addition to sodium MRI. Imaging hydrogen and sodium usually require two separate coils. However, coils are not generally made to work together. That means getting two images involves taking a person out of the MRI machine, changing coils, then putting them back in. This often leads to errors
in registering the relative position of the images for an accurate overlay. Having a dual-tuned coil so that the reposition of a person does not need to take place between image acquisitions minimizes errors in mis-registration. Therefore, a dual-tuned coil is critical for accurate sodium quantification in small structures.

Dual-tuned coils typically have homogeneity or SNR trade offs when compared to similar coils that are not dual tuned. This comparison shows that the sodium portion of the dual-tuned coil performs similar to the single-tune sodium coil of the same dimensions. The dual-tuned coil sacrifices the uniformity of the hydrogen portion of the coil to maintain the sodium signal quality. This is typically an acceptable sacrifice for sodium imaging.

I was an integral part of construction and tuning of the initial prototype dual-tuned coil at BYU. The dual-tuned nature of the coil makes tuning more complicated than a single tuned coil. Tuning the coil is an art that is assisted by understanding of the theory behind how the coil is working.

### 7.6 Water Fat Separation with Multiple Acquisition SSFP

Depicting the differences between the water and fat distribution in the body has application with liver disease. As the disease progresses, the liver gains a higher percentage of fat. The disease is diagnosed through imaging. Steady-state free-precession MRI is a fast acquisition technique. The goal with this technique is to accelerate the process of acquiring fat and water images for applications such as diagnosing liver disease.

My main contribution to the water fat separation with multiple acquisition SSFP was in experimental design and execution. Michael Mendoza is the masters student who took the lead on this project. He had no practical experience with MRI before this project so I provided crucial input for experiment design and practical ranges of parameters. This included MRI coil choice, phantom design, and programming the pulse sequence used. I also provided algorithm consultation and text revisions.
7.7 Quantitative MRI of Osteoarthritis for Multicenter Trials: Standardization between Different Centers and Manufacturers

The importance of this study may not be immediately obvious to those unfamiliar with MRI. There are three main whole body MRI vendors along with a handful of other smaller MRI vendors. There is no standardization among vendors that allows direct comparison of image intensity across different images, even on different machines in the same line of scanner. Some of the terminology between the different scanners is also different.

Differences can arise because of coil differences, subtle differences in how the pulse sequence was programmed, or differences in the settings of the sequence. If the coils differences and differences in how the pulse sequence was programmed were not an issue, then eliminating the differences in the settings of the pulse sequence would not be an issue. However, because of patents and proprietary technology
My contribution for the multicenter trials was crucial because I designed and had manufactured the phantom used both at BYU and Stanford. I also utilized my pulse sequence expertise to match the BYU pulse sequences to the Stanford pulse sequences as much as possible.

The phantom had to include a thin layer on the order of 1 mm with a variable thickness to mimic knee cartilage. It also needed fiducial markers for sodium of varying sodium concentrations as a reference to quantify the sodium concentration in other areas. An additional confounding factor is matching tissue parameters with the phantom material. I was able to do this through referencing older papers that studied phantom materials (agarose gel doped with CuSO4) at 1.5 T, extrapolate to 3T, then focus on the right concentrations with an experiment.

Matching the pulse sequences to those available at Stanford required some modification of the code for a custom pulse sequence not available on Siemens systems as well as making informed decisions as to the parameters that are crucial to match versus those parameters that should not make much difference.

7.8 **Relaxometry and Contrast Optimization for Laryngeal Imaging at 3 Tesla**

The Laryngeal Imaging project started with coil optimization by James Badal which I was peripherally involved with. From there it moved to porcine larynx imaging. I was integrally involved with preparing the specimen for imaging by fixing it in agarose gel to reduce the number of air-tissue interfaces that introduce susceptibility artifacts.

I have also been integrally involved in relaxometry measurements from specifying sequences and sequence parameters to recovering the $T_1$ and $T_2$ values from the images.

7.9 **Enhancing Diffusion Imaging with Non-linear Insert Gradients**

Diffusion imaging attempts to generate contrast based on the freedom of molecules to diffuse in the material being imaged. It is a negative contrast mechanism in MRI. This means that higher diffusion leads to lower signal level. This happens because a gradient is turned on to create inner-voxel dephasing. After a period of time, an equivalent but opposite gradient is turned on. If all the molecules are static during this period of time, then
Figure 7.8: Knee phantom designed for quantitative experiments: The kneeed phantom pictured has a compartment of variable thickness which is a hemisphere that ranges from 1mm thick at the peak to 3mm thick at the edges. It was immersed in an agarose solution for imaging and contained 4 vials of varying concentration sodium to aid in sodium quantitation. Part (a) shows the computer aided design of the knee phantom and part (b) shows the 3D printed section of the knee phantom.

all inner-voxel dephasing will be reversed. However, for any voxels that diffused to another part of the voxel or to another voxel altogether, the dephasing will not be reversed. This means that areas with a lot of diffusion happening will have residual dephased spins. These dephased spins lead to the lower signal level for tissues with significant amounts of diffusion.

Diffusion imaging suffers from low signal levels because of this negative contrast mechanism and because the diffusion gradients require a significant amount of time. During the time diffusions gradients are on, there is $T_2$ and possibly $T_2^*$ decay happening, depending on the method of diffusion imaging.

One way to shorten the time required for diffusion gradients is to maximize the gradient strength. Most MR imaging platforms use whole body linear gradients. This means that far from isocenter of the magnet, the linear gradient fields are changing much
more than close to isocenter. This means that there is a larger change in magnetic field over
time (dB/dt) in the periphery. At times, this can generate enough electrical current in small
nerves in the periphery to stimulate them. This is called peripheral nerve stimulation and
it is a concern. Generally the effect manifests itself as discomfort or skin twitching. This
limits the strength of the whole body gradients.

With a limited gradient strength, the only option is to allow more time for diffusion to
increase the diffusion weighting. However, more time for diffusion also leads to more signal
loss from the $T_2/T_2^*$ decay. This decreases the SNR in the resulting image which can effect
the utility of the acquired data. [75, 76]

Due to this gradient strength limit, our group in collaboration with the University of
Utah, explored the potential of having a smaller gradient set inside the magnet to enhance the
diffusion gradients. We showed that there is potential for increasing the signal-to-noise ratio
in diffusion imaging through using the insert gradients to get equivalent gradient strengths
in a shorter period of time. This allows for less $T_2$ decay before imaging which increases the
signal level. [32]

My contributions to this project included $T_1$ and $T_2$ mapping of the phantom, $B_1$
mapping, phantom design, and assisting with experiment design.
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Appendix A

Text of Selected Proceedings

This appendix contains the verbatim text from selected proceedings and one paper abstract that I contributed to as outlined in Chapter 7.

A.1 Ultra-Short TE (UTE) Imaging of Brain Lesions[27]

INTRODUCTION: The location and amount of proteins in the brain can be used to discriminate between different neurological diseases. However, it is very difficult to directly image proteins in the brain with MRI due to a very weak and rapidly decaying (short T2*) MR signal that is overwhelmed by the much stronger and longer-lasting (longer T2*) signal from other water components in the brain. Normal MRI techniques are not suitable for probing the signal of very short T2* tissues, since the signal from these tissues has typically decayed before it is sampled. Here, we explored the use of a custom 3D ultra-short TE (UTE) technique to detect signal from very short T2* tissue in an ex vivo brain with known Braak VI tauopathy. With the technique, we were able to detect the MR signal from tissues with T2* values of less than 1ms. We were further able to quantify both the T1 and T2* of the short-T2* tissues detected.

METHODS: We implemented a 3D UTE MRI sequence with a 3D cones k-space trajectory, and conducted ex vivo scans on a 3 Tesla scanner of a formalin fixed human temporal lobe from a subject with known Braak VI tauopathy, heaviest in the hippocampus and para hippocampal gyrus. We chose an area of the brain for our study that we expect to have high volume of beta amyloid and tau proteins. We then acquired the UTE images at TEs of 0.4, 0.6, 0.8, 1, 1.2, 1.5, 2, 2.5, 3, and 3.5ms and TR of 16ms. Resolution was 1mm isotropic and the FOV was 15 cm in all directions. Each of these scans was repeated at flip angles ranging from 5 to 60 degrees. Difference images were then formed by subtracting the TE=3.5ms images from the TE=0.4ms images, effectively suppressing longer T2* tissues. We defined four regions of interest (ROIs) in areas with visible short T2* signal in the hippocampus and then calculated an average T2* for each ROI by fitting the signal from each echo to a simple monoexponential curve. T1 was then estimated for each ROI by ascertaining which flip angle yielded the largest signal for the corresponding ROI, and applying the Ernst angle formula relating maximum signal to flip angle and T1.

RESULTS: We measured T2* values in the short T2* tissues at approximately 1.5 - 2.6ms for the ROIs having about 5-12 pixels. We hypothesize that these regions yielding short T2* MR signal correlate with areas with heavy Tau protein deposits. The T1 estimated in these
regions was approximately 300ms. Short T2* signal is detected both in areas around the hippocampus as well as around blood vessels.

CONCLUSION: A novel 3D UTE MRI sequence with a 3D cones k-space trajectory was used to image short T2* tissues in the hippocampus. Future work will seek to determine if the short T2* signal observed is water bound to protein deposits as hypothesized.

A.2 Phase-Sensitive Sodium $B_1$ Mapping Abstract

Quantitative sodium MRI requires accurate knowledge of factors affecting the sodium signal. One important determinant of sodium signal level is the transmit $B_1$ field strength. However, the low signal-to-noise ratio typical of sodium MRI makes accurate $B_1$ mapping in reasonable scan times challenging. A new phase-sensitive $B_1$ mapping technique has recently been shown to work better than the widely used dual-angle method in low-signal-to-noise ratio situations and over a broader range of flip angles. In this work, the phase-sensitive $B_1$ mapping technique is applied to sodium, and its performance compared to the dual-angle method through both simulation and phantom studies. The phase-sensitive method is shown to yield higher quality $B_1$ maps at low signal-to-noise ratio and greater consistency of measurement than the dual-angle method. An in vivo sodium $B_1$ map of the human breast is also shown, demonstrating the phase-sensitive method’s feasibility for human studies. Magn Reson Med, 2010. 2010 Wiley-Liss, Inc.

A.3 Performance Comparison of a Hybrid Dual-Tuned $^{23}$Na/$^1$H Birdcage to a Single-Tuned $^{23}$Na Birdcage with Identical Geometry

INTRODUCTION: Recent improvements in coil and gradient hardware, the availability of whole-body scanners with high polarizing field strengths, and the development of efficient pulse sequences with extremely short echo times have made feasible sodium MRI in vivo in reasonable scan times. These advances have rekindled interest in sodium MRI over the past decade for a variety of applications, including the assessment of cartilage health [1], characterization of tumors [2], detection of abnormal sodium levels in the kidneys [3], and assessment of tissue damage following stroke [4]. Dual-tuned 1H/23Na coil configurations (i.e., coils that resonate at both sodium and hydrogen frequencies) are highly desirable for many applications of sodium MRI. Sodium image acquisition can then be performed in conjunction with a standard 1H exam without the need to move the patient to change coils. This is particularly advantageous when accurate registration of sodium and proton images is required. Many dual-tuned coil designs employ frequency block traps, allowing selective routing of different frequencies through either spate rungs or rings in a birdcage structure. This approach suffers from significant inductive losses (due to wire resistance in the inductor) and magnetic field losses (due to inductors coupling to other structures or radiating in air), lowering coil electrical Q and SNR performance [5]. This work is based on a hybrid low-pass $^{23}$Na, high-pass 1H birdcage design (described by our collaborators at Stanford in a separate abstract) that employs multiple end rings in a single birdcage structure to make it dual resonant without frequency block traps [6]. The design incorporates a short z-FOV sodium quad low-pass birdcage in the central section of a split z-axis proton quad high-pass birdcage. High-pass birdcage coils are in general symmetric about the z-axis, with balanced currents
Figure A.1: Pictures of dual-tuned and single tuned coils: (a) Hybrid low-pass $^{23}$Na, high-pass $^1$H dual-resonant dual-quadrature coil, and (b) single-tuned low-pass $^{23}$Na quadrature birdcage with identical geometry to sodium (low-pass) section of dual-resonant design.

in opposite directions such that the addition of a ring at the z-axis center has no significant effect. In this study, we compare the sodium performance (SNR and B1 homogeneity) of the hybrid dual-resonant design to that of a single-tuned quadrature sodium birdcage coil with identical geometry to the sodium quadrature low-pass birdcage in the central section of the dual-resonant coil. Our results indicate that the sodium performance degradation of the dual-tuned design relative to the single-tuned sodium birdcage geometry is minimal.

**METHODS:** A hybrid low-pass sodium, high-pass hydrogen dual-resonant quadrature birdcage (Figure 1a) was built and tuned for both sodium and hydrogen imaging at 3T. Geometry of this dual-resonant birdcage was: inside diameter = 16 cm, inner end-ring separation (low-pass sodium) = 8.4 cm, outer end-ring separation (high-pass hydrogen) = 24.5 cm. A single-tuned low-pass sodium quadrature birdcage (Figure 1b) was then constructed with identical geometry to the inner (sodium) portion of the dual-resonant structure (inside diameter = 16 cm, end-ring separation = 8.4 cm), and tuned for sodium imaging at 3T. A uniform cylindrical phantom with $[Na+]$ of 150 mM was constructed to fit inside the coils. 3D sodium images of the phantom were then acquired (both magnitude images and B1 maps) with each coil using a custom EPI GRE sequence adapted for phase-sensitive sodium B1 mapping [7]. A region of interest was defined across a central portion of the phantom, and SNR measured across the ROI in sodium images from each coil. The standard deviation of the B1 map values across the sensitive region of the coils was also measured for each coil to give a measure of B1 homogeneity.

**RESULTS AND DISCUSSION:** Sodium magnitude images for a central slice through the phantom for each coil are shown in Figure 2, along with the measured SNR across the central region of interest. An SNR loss of less than 3% is observed in the dual-resonant structure relative to the single-resonant birdcage. B1 maps for a central slice are shown for
Figure A.2: **Magnitude sodium images from dual-tuned coil**: Magnitude sodium images, with SNR measurements across the indicated ROI. The dual-tuned design achieves nearly the same SNR performance as the single-tuned design.

Figure A.3: **Sodium $B_1$ maps**: Sodium $B_1$ maps (acquired with a phase-sensitive sodium EPI $B_1$ mapping technique). Both coil designs achieve very good $B_1$ homogeneity across the sensitive volume.
each coil in Figure 3. While there are some variations in the B1 maps between coils and the sensitive volume is apparently slightly smaller in the single-tuned design, the dual-resonant structure is only slightly less homogeneous for sodium than the single-tuned coil. Overall, dual-resonance is achieved in this hybrid design with remarkably little performance penalty for sodium imaging relative to a single-tuned sodium birdcage design. Future work will assess the performance of the 1H high-pass portion of the hybrid dual-resonant coil.

REFERENCES:

A.4 Water Fat Separation with Multiple Acquisition SSFP[26]

Introduction: Balanced steady-state free precession (bSSFP) MRI is a technique capable of producing images with high signal-to-noise ratio (SNR) in a short imaging time but suffers from bands of signal loss due to magnetic field inhomogeneity and susceptibility variations. These bands of signal loss degrade image quality. Several methods have been developed to remove these banding artifacts. The simplest methods combine images across multiple bSSFP image acquisitions. Reliable and uniform water fat separation, which can be used to improve medical diagnosis, is also a challenging problem. In many applications the water component is the primary signal of interest, while the fat component represents a signal that can obscure the underlying pathology or other features of interest. In other applications the fat signal is the signal of interest.

This work was motivated by the need for robust water fat separation and band reduction in the presence of field inhomogeneity when using bSSFP. In this work, we present a novel technique that combines the advantages of bSSFP with Dixon reconstruction in order to produce robust water fat decomposition with high SNR in a short imaging time, while simultaneously reducing banding artifacts that traditionally degrade image quality.

Theory: At large flip angles, the bSSFP signal level, as a function of off-resonance frequency, forms a sinusoidal-like spectral profile. This spectral profile can be arbitrarily shifted in frequency by increasing the phase of the RF pulse by a constant value, dphi, from excitation to excitation. When four phase-cycled bSSFP images are acquired with dphi = 0, 90, 80, and 270, they generate four evenly distributed signals along a bSSFP spectrum (Figure 1). On a voxel-by-voxel basis, the three greatest magnitude signals from these images, which are located in the pass band region, are combined to generate a more homogenous signal with reduced banding artifacts.

The choice of echo time (TE) effects the relative phase between water and fat components due to the chemical shift. For a given difference in resonance frequency between water and fat (CS), the time between successive images (dt) is selected to generate “in-phase” images (images with a 0, or 2pi phase difference) and “out-of-phase” images (images with a pi phase difference). A time difference between images equal to odd integer multiples of 1/(2*CS) is used to generate “in-phase” images, while a time difference equal to even integer multiples of 1/(2CS) is utilized to produce “out-of-phase” images. Linear combinations of
Figure A.4: Phantom demonstration of SSFP fat water separation: Simulated oil/water phantom (top) and real oil/water experiments (bottom) demonstrating water fat separation with multiple-acquisition bSSFP. (a-d) Four-cycled images with $\delta \phi = 0^\circ, 90^\circ, 180^\circ, 270^\circ$. (d) Estimated water image. (e) Estimated fat image.

These images, according to Dixon reconstruction, can be used to produce separate water and fat images.

These two ideas form the basis for Water Fat Separation with Multiple-Acquisition bSSFP. This algorithm utilizes four phase-cycled bSSFP acquisitions at specific echo times to generate “in-phase” and “out-of-phase” images. Linear combinations of the highest magnitude signals from these images are used to produce separate water and fat images.

**Methods:** Four phase cycled bSSFP images of an oil/water phantom were generated by both a bSSFP simulation and by a 3T Siemens scanner. The common bSSFP parameters for all images were: flip angle=90 degrees and $TR = 10 \text{ms}$. The respective parameters for each of the four phase-cycled images (Figure 2a-d) were: $d\phi = 0, 90, 180, 270^\circ$ and $TE = 3.25 \text{ms}, 4.42 \text{ms}, 5.58 \text{ms} \text{ and } 6.75 \text{ms}$. Images were reconstructed on a voxel-by-voxel basis.

**Results and Discussion:** The simulated and acquired results for an oil/water phantom are shown in Figure 2. The first four images in each series are the generated phase-cycled images, while the last two are water and fat images respectively. Note reduction of the fat component in the water image and the reduction of the water component in the fat image. These results are promising, in reasonable agreement with theory and show that the algorithm is capable of water fat separation in the presence of SSFP banding artifacts due to field inhomogeneity. While, capable of water fat separation, the reconstruction method is not yet robust in the presence of strong field inhomogeneities that produce a large number of banding artifacts in bSSFP. Further work will explore methods for eliminating these errors.

A.5 Quantitative MRI of Osteoarthritis for Multicenter Trials: Standardization between Different Centers and Manufacturers[30]

**Introduction:** Quantitative magnetic resonance imaging (qMRI) is a powerful tool which shows great promise in providing biomarkers for early detection of osteoarthritis (OA) and
Figure A.5: bSSFP signal as a function of off-resonance frequency at large tip angle: Selecting four evenly distributed points along one cycle of a bSSFP spectrum places only one point at a signal null.

for evaluating cartilage response to disease-modifying OA drugs. Quantitative measurement of cartilage morphometry provides information about cartilage area, thickness, and volume, while compositional parameters based on cartilage relaxation times and sodium content provide valuable information regarding degradation of the cartilage extracellular matrix. A variety of sequences and coils across several manufacturers have been developed to measure these cartilage parameters, each with their own strengths as well as inherent biases. This makes evaluation of each of these tissue parameters difficult across multicenter trials. One study examined reproducibility of cartilage morphology and T2 and T1rho relaxation times across sites and platforms and found greater reproducibility of morphology as compared to T2 and T1rho. Reproducibility of sodium MR has not been assessed across platforms. In this work we assess the repeatability and reproducibility of cartilage morphometry, T2, and sodium concentration qMRI measurements intra-site and between sites and manufacturers.

Methods: MRI Scanning: Imaging experiments were performed at two research sites on Siemens Tim Trio (Siemens Medical Systems, Erlangen, Germany) and GE MR 750 (GE Healthcare, Milwaukee, WI) 3T whole body MRI scanners. A phantom, with 5 cylindrical compartments and one cartilage-like layer, was designed in CAD and then 3D printed (figure 1). The compartments were filled with solutions of varying concentrations of sodium chloride and agarose to create variable sodium and T2 relaxation values across compartments. The imaging protocol at each site included a 3D double echo steady-state (DESS) sequence.
(TR = 16.3 ms, TE = 4.7/11.3 ms, flip angle (FA) = 25, 0.6x0.5x0.7 mm resolution) for morphometry and a multi-echo spin echo (MESE) sequence with seven echo times from 10.6 ms to 73 ms (TR = 2.7s, 0.6x0.4x3.0 mm resolution) for T2 measurement. Sodium images were obtained using a fast gradient-spoiled sequence with the 3D cones k-space trajectory (TR/TE = 35/0.6 ms, FA = 70, 28 signal averages). The imaging protocol at each site consisted of 5 randomized scan blocks with phantom repositioning between each block. Each sequence was repeated twice consecutively, per scan block, giving a total of 10 scans per sequence, per site. Analysis: T2 relaxation times were calculated using a mono-exponential fit in OsiriX. Morphometric measurements consisted of an area calculation of each compartment. Sodium concentrations were assessed with ratiometric analysis; the compartment with the largest sodium concentration ([250 mM]) was used as the control. For consistency, each respective quantitative measure for both sites was analyzed by a single individual. The repeatability of each sequence at each site, and reproducibility of each sequence between sites, was assessed using the Bland-Altman method and calculation of the concordance correlation.

**Results and Discussion:** Bland-Altman plots for intra-scan differences in morphometric measurements, calculated sodium concentrations, and calculated T2 relaxation times in each phantom compartment across the two sites showed good agreement (Figure 2). A high concordance correlation coefficient (CC) was observed between intra-site measurements of phantom morphometry, T2 relaxation times, and sodium concentrations for each site (Table 1). This implies that within a given site, quantitative measurements of tissue morphometry, T2, and sodium concentration are repeatable. A high concordance correlation coefficient (CC = 0.967) was also observed between the two sites for morphometric measurements suggesting that quantitative morphometric measurements can accurately be assessed between imaging sites. Sodium concentration measurements were significantly higher at site 1 compared to site 2 (p<0.001), leading to low reproducibility (CC=0.749). However, a high correlation coefficient (r=0.956) suggests that the difference might be readily correctable. The sequence used for sodium image acquisition was written in house and is identical between sites. Thus biases in sodium quantification may be due to MR hardware differences between sites which may be accounted for. MESE T2 measurements were not reproducible between sites and had a very low correlation. Variations in the T2 mapping sequences may introduce a bias in T2 measurements5. This study employed manufacturers product MESE sequences that differ in radiofrequency and gradient pulses that limited our ability to standardize the scan parameters. Along with their inherent biases, the different sequences likely have contributed to the low correlation in T2 values between sites.

**Conclusion:** Correlation is high for morphologic imaging between sites with different manufacturers. For sodium MR with identical imaging sequences at both sites, a correctable bias is introduced, likely due to hardware differences. However, use of different acquisition sequences on different platforms for T2 measurements showed errors that are not easily correctable. For standardization of quantitative MRI of OA between sites, nearly identical software is likely required.
Table A.1: Intra-Site Correlation

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A.6 Relaxometry and Contrast Optimization for Laryngeal Imaging at 3 Tesla[31]

Introduction: Accurate models of vocal fold biomechanics and vibration can be used to study voice physics and to guide clinicians in their choice of treatment options as they at-
Figure A.7: Bland-Altman plots of intra-scan differences across the 2 sites
tempt to restore or preserve voice quality in persons suffering from vocal or speech disorders. The development of engineered tissue and voice prostheses to replace damaged vocal fold tissues could benefit from these models. In addition, post-operative function and voice quality can be studied in order to guide phonosurgical interventions. The development of accurate models of vocal fold biomechanics would benefit from high-resolution 3D images with sufficient contrast between the various tissues of interest. While CT has been explored to develop these models in the past, it suffers from very limited soft-tissue contrast for differentiating the component tissues of the larynx. In this study, we designed and built a 2-channel phased-array receive-only coil for high-resolution imaging of the larynx. The coil was tested on an excised pig larynx. T1 and T2 relaxometry was performed on an excised pig larynx to understand the MR signal characteristics of various tissues in the larynx. These values were then used to choose optimal sequence parameters for maximizing contrast between the comus elasticus tissue and the mucosa tissue, two tissues that are important (but difficult) to distinguish for accurate biomechanical modeling of laryngeal function.

Methods: A custom 2-channel receive-only phased array coil was designed to lie in close proximity to the larynx, improving signal detection across the tissues of interest. The coil was tested on an excised pig larynx set in agarose gel to minimize susceptibility artifact. T2 measurements were then performed on the pig larynx using a single-echo spin-echo sequence with TEs of 17, 30, 45, 75, 90, 120, and 200 ms. A variety of tissues were segmented in the images (mucosa, comus elasticus, cricoid lamina, posterior cricoarytenoid, vocal folds, and thyroid cartilage), and average T2 values calculated for each tissue using a simple monoexponential fit. T1 measurements were then performed using an inversion-recovery sequence with TR/TE = 5000/5.23 ms and inversion times TI = 50, 300, 700, 1200, and 2000 ms. Tissues of interest were again segmented, and average T1 values calculated using a standard monoexponential model of T1 recovery. Following these measurements, a Bloch simulation of a 3D FLASH sequence was used to optimize the contrast for high-resolution 3D imaging of the larynx. The most difficult tissues to distinguish due to their relatively similar T1 and T2 values are mucosa and comus elasticus. A numerical optimization algorithm was used in conjunction with our measured T1 and T2 values for these two tissues and the Bloch simulation in an attempt to identify sequence parameters that maximize the contrast between mucosa and comus elasticus.

Results: Figure one shows a high-resolution image of the excised pig larynx with the various tissues of interest labeled. Table 1 summarizes the relaxometry results for each tissue. The T1 and T2 values for the cricoid lamina tissue falls in the range given in the literature for cartilage. (1) T1 and T2 measurements for most of the remaining tissues have not been previously reported at 3 Tesla. Ultimately, we hope to produce high-resolution images of the larynx in vivo using respiratory gating to minimize motion artifact. A very short TR is thus desirable to minimize acquisition time during each respiratory cycle. At TR/TE = 3.6/1.8 ms (a reasonable parameter set for 3D FLASH at the resolution and FOV we hope to achieve in vivo), our simulations showed that a flip angle of 9 degrees maximizes contrast between the mucosa and the comus elasticus tissues (Figure 2).
Table A.2: Pig Larynx $T_1$ and $T_2$ measurements at 3T in milliseconds (value +/- standard deviation)

<table>
<thead>
<tr>
<th>Tissue</th>
<th>$T_2$ (ms)</th>
<th>$T_1$ (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosa</td>
<td>110.2 +/- 16.3</td>
<td>1266.6 +/- 57.8</td>
</tr>
<tr>
<td>Comus Elasticus</td>
<td>79.3 +/- 9.8</td>
<td>1318.8 +/- 59.9</td>
</tr>
<tr>
<td>Cricoid Lamina (cartilage)</td>
<td>33.4 +/- 8.2</td>
<td>1023 +/- 74.6</td>
</tr>
<tr>
<td>Posterior Cricoarytenoid</td>
<td>33.5 +/- 5.4</td>
<td>965.9 +/- 39.2</td>
</tr>
<tr>
<td>Vocal Folds</td>
<td>59 +/- 7</td>
<td>1130.5 +/- 128.2</td>
</tr>
<tr>
<td>Thryoide Cartilage</td>
<td>67.7 +/- 8.7</td>
<td>991.2 +/- 13.5</td>
</tr>
</tbody>
</table>

Conclusion: Accurate models of vocal fold biomechanics require high-resolution 3D images with excellent soft tissue contrast. In this study, we were able to demonstrate high-resolution laryngeal imaging at 3 Tesla in an excised pig larynx using a custom laryngeal phased array receive-only coil. We then used the coil to perform high-resolution relaxometry on an excised pig larynx to obtain average T1 and T2 values of the critical tissues for modeling laryngeal function. These values were used to optimize sequence parameters for maximizing contrast between difficult-to-distinguish tissues in the larynx.

Figure A.9: Signal difference between the Mucosa tissue and the Comus Elasticus tissue for a 3D FLASH sequence.
Appendix B

Dual Echo in the Steady State (DESS) Pulse Sequence Signal Derivation Accounting for Diffusion

A derivation of the signal for a DESS like sequence is presented in Wu and Buxton [78]. However, many of the steps in the derivation are glossed over and were not easy for me to understand from one step to another. I present a more detailed derivation going through some of the steps that were most obscure to me. Wu and Buxton base their derivation on a pulse sequence with a single pulsed gradient between the RF pulses. A previous work by Kaiser and Ernst [79] derived a steady state signal in the presence of a constant gradient. The Wu and Buxton derivation differs by using a pulsed gradient instead of a constant gradient. Using a pulsed gradient creates the need for solving for three different time periods: the period before the pulsed gradient, the period during the pulsed gradient, and the period after the pulsed gradient.

The signal derivation for the transverse magnetization of all three signal periods start with the Bloch equation which accounts for diffusion [80],

\[
\frac{\partial M^+(\vec{r},t)}{\partial t} = \left( -j\gamma \vec{G} \cdot \vec{r} - \frac{1}{T_2} \right) M^+(\vec{r},t) + D\nabla^2 M^+(\vec{r},t),
\]  

(B.1)

where the definition of the Laplacian, \(\nabla^2\), is

\[
\nabla^2 \mu(\Theta,t) = \frac{\partial^2 \mu(\Theta,t)}{\partial x^2} + \frac{\partial^2 \mu(\Theta,t)}{\partial y^2} + \frac{\partial^2 \mu(\Theta,t)}{\partial z^2}.
\]  

(B.2)

The position-dependent angle of precession is

\[
\Theta(\vec{r}) = -\gamma \vec{G} \cdot \vec{r},
\]  

(B.3)

assuming the pulsed gradient, \(\vec{G}\), is the only source for the angle of precession.

Wu and Buxton follow the same approach as Kaiser when solving (B.1). First, assume the magnetization is a function of the magnetic moment with an exponential decay term. Then, using that magnetization along with (B.2) and (B.3), simplify (B.1). Next, express the solution as a Fourier integral of the product of two terms: an unknown function and an exponential term with an unknown exponent. Then, substitute that form of the solution into the simplified Bloch-Torrey equation to solve for the unknown exponent. Boundary conditions and the steady state condition lead to solution for the other unknown terms. Finally, the signal level is calculated as the mean of individual magnetizations with a spread of angles caused by the pulsed gradient.
First, I will derive the solution for the transverse magnetization in each time period. Then, I will follow a similar procedure to solve the longitudinal magnetization.

B.1 Transverse Magnetization Solution

Solution to the transverse magnetization comes in three parts: one for each time period. Following those partial solutions, boundary conditions and the steady state condition provide the remaining parts of the solution. For the first time period, I will include much more detail than the following time periods. Although, in all time periods I aim to include enough detail to follow the derivation without any major jumps or handwaving.

B.1.1 Time Period Prior to Pulsed Gradient

Magnetization as a function of magnetic moment: Magnetization $M^+$ before the pulsed field gradient may be represented by the net magnetic moment $\mu$ attenuated by $T_2$ decay as

$$M^+(\vec{r}, t) = \mu(\Theta, t)e^{-t/T_2}. \quad (B.4)$$

Substituting (B.4) into (B.1) yields

$$\frac{\partial \mu(\Theta, t)e^{-t/T_2}}{\partial t} = \left(-j\gamma\vec{G} \cdot \vec{r} - \frac{1}{T_2}\right)\mu(\Theta, t)e^{-t/T_2} + D\nabla^2 \mu(\Theta, t)e^{-t/T_2}. \quad (B.5)$$

Through simplifying pieces of the equation separately, the answer may be understood better. Starting with the left hand side of the equation,

$$\frac{\partial \mu(\Theta, t)e^{-t/T_2}}{\partial t} = \mu(\Theta, t)\frac{\partial e^{-t/T_2}}{\partial t} + \frac{\partial \mu(\Theta, t)}{\partial t}e^{-t/T_2}$$

$$\frac{\partial}{\partial t} e^{-t/T_2} = \mu(\Theta, t)\frac{\partial}{\partial t} e^{-t/T_2}$$

$$\frac{\partial}{\partial t} e^{-t/T_2} = \mu(\Theta, t)\frac{\partial}{\partial t} e^{-t/T_2}$$

$$\frac{\partial \mu(\Theta, t)e^{-t/T_2}}{\partial t} = \mu(\Theta, t)\left(-\frac{1}{T_2}\right) + \frac{\partial \mu(\Theta, t)}{\partial t}e^{-t/T_2}. \quad (B.6)$$

Moving to the Laplacian, solving for the partial derivatives of $x$ first

$$\frac{\partial^2 \mu(\Theta, t)}{\partial x^2} = \frac{\partial}{\partial x} \frac{\partial \mu(\Theta, t)}{\partial x}$$

$$= \frac{\partial}{\partial x} \left(\frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{\partial \Theta}{\partial x}\right)$$

$$= \frac{\partial^2}{\partial x^2} \mu(\Theta, t) + \frac{\partial}{\partial x} \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} \frac{\partial \Theta}{\partial x}$$

$$= \frac{\partial^2}{\partial x^2} \mu(\Theta, t) + \frac{\partial^2}{\partial \Theta^2} \left(\frac{\partial \Theta}{\partial x}\right)^2. \quad (B.7)$$
where

\[
\frac{\partial \Theta}{\partial x} = - \frac{\partial \gamma \vec{G} \cdot \vec{r}_\tau}{\partial x} = - \frac{\partial \gamma (G_x \hat{i} + G_y \hat{j} + G_z \hat{k}) \cdot (x \hat{i} + y \hat{j} + z \hat{k})}{\partial x} = - \frac{\partial \gamma (G_x x + G_y y + G_z z)}{\partial x} = - \gamma G_x \tau
\]  

(B.8)

and

\[
\frac{\partial^2 \Theta}{\partial^2 x} = \frac{\partial}{\partial x} \frac{\partial \Theta}{\partial x} = - \frac{\partial \gamma G_x \tau}{\partial x} = 0.
\]  

(B.9)

Likewise, the partial derivatives of \(y\) and \(z\) parallel that of \(x\) resulting with

\[
\frac{\partial \Theta}{\partial y} = - \gamma G_y \tau
\]  

(B.10)

\[
\frac{\partial \Theta}{\partial z} = - \gamma G_z \tau
\]  

(B.11)

and

\[
\frac{\partial^2 \Theta}{\partial y^2} = 0
\]  

(B.12)

\[
\frac{\partial^2 \Theta}{\partial z^2} = 0.
\]  

(B.13)

Again, following the same process as (B.7)

\[
\frac{\partial^2 \mu(\Theta, t)}{\partial y^2} = \frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{\partial^2 \Theta}{\partial y^2} + \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} \left( \frac{\partial \Theta}{\partial y} \right)^2
\]  

(B.14)

and

\[
\frac{\partial^2 \mu(\Theta, t)}{\partial z^2} = \frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{\partial^2 \Theta}{\partial z^2} + \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} \left( \frac{\partial \Theta}{\partial z} \right)^2.
\]  

(B.15)

Then, substituting (B.8)-(B.13) into (B.7), (B.14), and (B.15),

\[
\frac{\partial^2 \mu(\Theta, t)}{\partial x^2} = \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} (\gamma G_x \tau)^2,
\]  

(B.16)

\[
\frac{\partial^2 \mu(\Theta, t)}{\partial y^2} = \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} (\gamma G_y \tau)^2,
\]  

(B.17)

\[
\frac{\partial^2 \mu(\Theta, t)}{\partial z^2} = \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} (\gamma G_z \tau)^2.
\]  

(B.18)
Next, substituting into (B.2) it becomes

\[
\nabla^2 \mu(\Theta, t) = \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} (\gamma G_x \tau)^2 + \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} (\gamma G_y \tau)^2 + \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} (\gamma G_z \tau)^2
\]

\[
= \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} \gamma^2 \tau^2 \left[G_x^2 + G_y^2 + G_z^2\right]
\]

\[
= \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} \gamma^2 \tau^2 G^2,
\]

where

\[
G^2 = G_x^2 + G_y^2 + G_z^2.
\]

Finally, using the pieces from (B.4) (B.6) and (B.19) and realizing that \( \vec{G} \) is zero, (B.1) for the time period before the gradient pulse is

\[
\frac{\partial \mu(\Theta, t)}{\partial t} e^{-t/T_2} = -\frac{1}{T_2} \mu(\Theta, t) e^{-t/T_2} + D \nabla^2 \mu(\Theta, t) e^{-t/T_2} + De^{-t/T_2} \nabla^2 \mu(\Theta, t)
\]

\[
-\frac{1}{T_2} \mu(\Theta, t) e^{-t/T_2} + \frac{\partial \mu(\Theta, t)}{\partial t} e^{-t/T_2} = -\frac{1}{T_2} \mu(\Theta, t) e^{-t/T_2} + D e^{-t/T_2} \nabla^2 \mu(\Theta, t)
\]

\[
\frac{\partial \mu(\Theta, t)}{\partial t} e^{-t/T_2} = D e^{-t/T_2} \nabla^2 \mu(\Theta, t)
\]

\[
\frac{\partial \mu(\Theta, t)}{\partial t} e^{-t/T_2} = D e^{-t/T_2} \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} \gamma^2 \tau^2 G^2
\]

\[
\frac{\partial \mu(\Theta, t)}{\partial t} e^{-t/T_2} = D(\gamma G \tau)^2 \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2}.
\]

**Solution as a Fourier Integral:** Now that (B.1) is simplified into (B.21) for the first time period, the solution may be represented as a Fourier integral of the form

\[
\mu(\Theta, t) = \int_{-\infty}^{+\infty} a(k)e^{A}e^{jk\Theta}dk,
\]

where \( a(k) \) and \( A \) are unknown functions. Equation (B.22) may be substituted into (B.21) to solve for one of those unknowns, \( A \). Approaching the left and right hand sides of (B.21) one at a time will provide a derivation that is more clear. Starting with the left hand side,

\[
\frac{\partial \mu(\Theta, t)}{\partial t} e^{-t/T_2} = \frac{\partial}{\partial t} \int_{-\infty}^{+\infty} a(k)e^{A}e^{jk\Theta}dk
\]

\[
= \int_{-\infty}^{+\infty} a(k) \frac{\partial e^{A}}{\partial t} e^{jk\Theta}dk
\]

\[
= \int_{-\infty}^{+\infty} a(k)e^{A} \frac{\partial A}{\partial t} e^{jk\Theta}dk.
\]
where all time dependence is assumed to be in $A$. Moving on to the right hand side, ignoring extra constants for the time being,

$$
\frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} = \frac{\partial^2}{\partial \Theta^2} \int_{-\infty}^{+\infty} a(k) e^{A e^{j k \Theta}} dk
$$

$$
= \frac{\partial}{\partial \Theta} \int_{-\infty}^{+\infty} a(k) e^{A} \frac{\partial e^{j k \Theta}}{\partial \Theta} dk
$$

$$
= \frac{\partial}{\partial \Theta} \int_{-\infty}^{+\infty} a(k) e^{A} e^{j k \Theta} \frac{\partial j k \Theta}{\partial \Theta} dk
$$

$$
= \frac{\partial}{\partial \Theta} \int_{-\infty}^{+\infty} a(k) e^{A} e^{j k \Theta} j k dk
$$

$$
= \int_{-\infty}^{+\infty} a(k) e^{A} e^{j k \Theta} j k dk
$$

$$
= \int_{-\infty}^{+\infty} a(k) e^{A} e^{j k \Theta} (j k)^2 dk
$$

$$
= - \int_{-\infty}^{+\infty} a(k) e^{A} e^{j k \Theta} k^2 dk,
$$

(B.24)

where $a(k)$ and $A$ are independent of $\Theta$ due to the nature of a Fourier transform. Then, substituting (B.23) and (B.24) into (B.21) it becomes

$$
\int_{-\infty}^{+\infty} a(k) e^{A} \frac{\partial A}{\partial t} e^{j k \Theta} dk = -D(\gamma G\tau)^2 \int_{-\infty}^{+\infty} a(k) e^{A} e^{j k \Theta} k^2 dk
$$

$$
\int_{-\infty}^{+\infty} a(k) e^{A} \frac{\partial A}{\partial t} e^{j k \Theta} dk = - \int_{-\infty}^{+\infty} D(\gamma G\tau)^2 a(k) e^{A} e^{j k \Theta} k^2 dk
$$

$$
0 = \int_{-\infty}^{+\infty} a(k) e^{A} \frac{\partial A}{\partial t} e^{j k \Theta} dk + \int_{-\infty}^{+\infty} D(\gamma G\tau)^2 a(k) e^{A} e^{j k \Theta} k^2 dk
$$

$$
0 = \int_{-\infty}^{+\infty} a(k) e^{A} e^{j k \Theta} (\frac{\partial A}{\partial t} + D(\gamma G\tau)^2 k^2) dk.
$$

(B.25)

This requirement may be satisfied with

$$
0 = \frac{\partial A}{\partial t} + D(\gamma G\tau)^2 k^2
$$

$$
\frac{\partial A}{\partial t} = -D(\gamma G\tau)^2 k^2
$$

$$
A = -D(\gamma G\tau)^2 k^2 t.
$$

(B.26)

Further conditions will facilitate solving for $a(k)$. However, partial solutions to the other time periods and longitudinal magnetization need to be found first.
B.1.2 Time Period During Pulsed Gradient

As a thorough example was given for the prior time period, I will skip some more obvious steps in this derivation.

**Magnetization as a function of magnetic moment:** Magnetization $M^+$ before the pulsed field gradient may be represented by the net magnetic moment $\mu$ attenuated by $T_2$ decay and signal decay due to diffusion as

$$M^+ (\vec{r}, t) = \mu(\Theta, t)e^{j\Theta(\vec{r})(t-\epsilon)/\tau-t/T_2}. \quad (B.27)$$

Substituting (B.27) into (B.1) yields

$$\frac{\partial \mu(\Theta, t)e^{j\Theta(\vec{r})(t-\epsilon)/\tau-t/T_2}}{\partial t} = \left( -j\gamma \vec{G} \cdot \vec{r} - \frac{1}{T_2} \right) \mu(\Theta, t)e^{j\Theta(\vec{r})(t-\epsilon)/\tau-t/T_2}$$

$$+ D \nabla^2 \mu(\Theta, t)e^{j\Theta(\vec{r})(t-\epsilon)/\tau-t/T_2}. \quad (B.28)$$

Through simplifying pieces of the equation separately, the answer may be understood better. Starting with the left hand side of the equation,

$$\frac{\partial \mu(\Theta, t)e^{j\Theta(\vec{r})(t-\epsilon)/\tau-t/T_2}}{\partial t} = \mu(\Theta, t) \frac{\partial e^{j\Theta(\vec{r})(t-\epsilon)/\tau-t/T_2}}{\partial t} + \frac{\partial \mu(\Theta, t)}{\partial t} e^{j\Theta(\vec{r})(t-\epsilon)/\tau-t/T_2}$$

$$= \left[ \mu(\Theta, t) \left( -j\frac{\Theta(\vec{r})}{\tau} - \frac{1}{T_2} \right) + \frac{\partial \mu(\Theta, t)}{\partial t} \right] e^{j\Theta(\vec{r})(t-\epsilon)/\tau-t/T_2} \quad (B.29)$$
Moving to the Laplacian, solving for the partial derivatives of $x$ first

\[
\frac{\partial^2 \mu(\Theta, t) e^{j\Theta(\vec{r}(t-\epsilon))/\tau-t/T_2}}{\partial x^2} = \frac{\partial}{\partial x} \left( \frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{\partial \Theta}{\partial x} + j \mu(\Theta, t) \frac{\partial \Theta(t-\epsilon)}{\partial x} \right) e^{j\Theta(t-\epsilon)/\tau-t/T_2}
\]

\[
= \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} \left( \frac{\partial \Theta}{\partial x} \right)^2 + j \frac{\partial \mu(\Theta, t)}{\partial \Theta} \left( \frac{\partial \Theta}{\partial x} \right)^2 \frac{(t-\epsilon)}{\tau} + j \frac{\partial \Theta(t-\epsilon)}{\partial x} \left( \frac{\partial \Theta}{\partial x} \frac{\partial \Theta}{\partial x} + j \mu(\Theta, t) \frac{\partial \Theta(t-\epsilon)}{\partial x} \right) \right) e^{j\Theta(\vec{r}(t-\epsilon))/\tau-t/T_2}
\]

\[
= \left( \frac{\partial \Theta}{\partial x} \right)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{(t-\epsilon)}{\tau} \right) - \mu(\Theta, t) \left( \frac{t-\epsilon}{\tau} \right)^2 e^{j\Theta(\vec{r}(t-\epsilon))/\tau-t/T_2}
\]

\[
= (\gamma G_x \tau)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{(t-\epsilon)}{\tau} - \mu(\Theta, t) \left( \frac{t-\epsilon}{\tau} \right)^2 \right) e^{j\Theta(\vec{r}(t-\epsilon))/\tau-t/T_2},
\]

where (B.8) and (B.9) are used as before. Again, following the same process as (B.30)

\[
\frac{\partial^2 \mu(\Theta, t) e^{j\Theta(\vec{r}(t-\epsilon))/\tau-t/T_2}}{\partial y^2} = (\gamma G_y \tau)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{(t-\epsilon)}{\tau} - \mu(\Theta, t) \left( \frac{t-\epsilon}{\tau} \right)^2 \right) e^{j\Theta(\vec{r}(t-\epsilon))/\tau-t/T_2},
\]

and

\[
\frac{\partial^2 \mu(\Theta, t) e^{j\Theta(\vec{r}(t-\epsilon))/\tau-t/T_2}}{\partial z^2} = (\gamma G_z \tau)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{(t-\epsilon)}{\tau} - \mu(\Theta, t) \left( \frac{t-\epsilon}{\tau} \right)^2 \right) e^{j\Theta(\vec{r}(t-\epsilon))/\tau-t/T_2}.
\]
Next, substituting into (B.2) it becomes
\[
\nabla^2 \mu(\Theta, t) = (\gamma G \tau)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{(t - \epsilon)}{\tau} - \mu(\Theta, t) \left( \frac{t - \epsilon}{\tau} \right)^2 \right) \times e^{j \Theta(\vec{r}(t-\epsilon)/\tau-t/T_2}. \tag{B.33}
\]

Finally, using the pieces from (B.27), (B.29), and (B.33), (B.1) for the time period during the gradient pulse is
\[
\frac{\partial \mu(\Theta, t)}{\partial t} e^{j \Theta(\vec{r}(t-\epsilon)/\tau-t/T_2)} = D (\gamma G \tau)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{(t - \epsilon)}{\tau} - \mu(\Theta, t) \left( \frac{t - \epsilon}{\tau} \right)^2 \right) \times e^{j \Theta(\vec{r}(t-\epsilon)/\tau-t/T_2}. \tag{B.34}
\]

\[
\frac{\partial \mu(\Theta, t)}{\partial t} = D (\gamma G \tau)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} \frac{(t - \epsilon)}{\tau} - \mu(\Theta, t) \left( \frac{t - \epsilon}{\tau} \right)^2 \right). \tag{B.35}
\]

**Solution as a Fourier Integral:** Now that (B.1) is simplified into (B.35) for the first time period, the solution may be represented as a Fourier integral of the form
\[
\mu(\Theta, t) = \int_{-\infty}^{+\infty} a'(k) e^{A' e^{jk\Theta}} dk, \tag{B.36}
\]
where \(a'(k)\) and \(A'\) are unknown functions, as before. Equation (B.36) may be substituted into (B.35) to solve for one of those unknowns, \(A'\). Approaching the left and right hand sides of (B.35) one at a time will provide a derivation that is more clear. Starting with the left hand side,
\[
\frac{\partial \mu(\Theta, t)}{\partial t} = \int_{-\infty}^{+\infty} a'(k) e^{A' \frac{\partial A'}{\partial t} e^{jk\Theta}} dk, \tag{B.37}
\]
where all time dependence is again assumed to be in \(A'\). Moving on to the right hand side, starting with the single derivative
\[
\frac{\partial \mu(\Theta, t)}{\partial \Theta} = \int_{-\infty}^{+\infty} a'(k) e^{A' e^{jk\Theta} j k} dk. \tag{B.38}
\]
Then, moving to the second derivative
\[
\frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} = -\int_{-\infty}^{+\infty} a'(k) e^{A' e^{jk\Theta} k^2} dk. \tag{B.39}
\]
Next, substituting (B.36), (B.37), (B.38), and (B.39) into (B.35) it becomes

\[
\int_{-\infty}^{+\infty} a'(k) e^{A'} \frac{\partial A'}{\partial t} e^{jk\Theta} dk = D (\gamma G \tau)^2 \left( - \int_{-\infty}^{+\infty} a'(k) e^{A'} e^{jk\Theta} k^2 dk \right.
\]
\[
+ 2j \int_{-\infty}^{+\infty} a'(k) e^{A'} e^{jk\Theta} jk \frac{(t - \epsilon)}{\tau} \right.
\]
\[
- \int_{-\infty}^{+\infty} a'(k) e^{A'} e^{jk\Theta} dk \left( \frac{t - \epsilon}{\tau} \right)^2 \right) \tag{B.40}
\]

\[
\int_{-\infty}^{+\infty} a'(k) e^{A'} \frac{\partial A'}{\partial t} e^{jk\Theta} dk
\]
\[
= - \int_{-\infty}^{+\infty} D (\gamma G \tau)^2 a'(k) e^{A'} \left( k^2 + 2k \frac{(t - \epsilon)}{\tau} + \left( \frac{t - \epsilon}{\tau} \right)^2 \right) e^{jk\Theta} dk \tag{B.41}
\]

\[
\int_{-\infty}^{+\infty} a'(k) e^{A'} \left[ \frac{\partial A'}{\partial t} + D (\gamma G \tau)^2 \left( k^2 + 2k \frac{(t - \epsilon)}{\tau} + \left( \frac{t - \epsilon}{\tau} \right)^2 \right) \right] e^{jk\Theta} dk = 0. \tag{B.42}
\]

This requirement may be satisfied with

\[
0 = \frac{\partial A'}{\partial t} + D (\gamma G \tau)^2 \left( k + \frac{t - \epsilon}{\tau} \right)^2
\]
\[
\frac{\partial A'}{\partial t} = -D (\gamma G \tau)^2 \left( k + \frac{t - \epsilon}{\tau} \right)^2 \tag{B.43}
\]
\[
A' = \frac{-\tau}{3} D (\gamma G \tau)^2 \left( k + \frac{t - \epsilon}{\tau} \right)^3.
\]

### B.1.3 Time Period After Pulsed Gradient

As a thorough example was given for the prior time period, I will skip some more obvious steps in this derivation.

**Magnetization as a function of magnetic moment:** Magnetization \(M^+\) after the pulsed field gradient may be represented by the net magnetic moment \(\mu\) attenuated by \(T_2\) decay and signal decay due to diffusion as

\[
M^+(\vec{r}, t) = \mu(\Theta, t) e^{j\Theta(\vec{r}) - t/T_2}. \tag{B.44}
\]

Substituting (B.44) into (B.1) yields

\[
\frac{\partial \mu(\Theta, t) e^{j\Theta(\vec{r}) - t/T_2}}{\partial t} = \left( -jG \vec{G} \cdot \vec{r} - \frac{1}{T_2} \right) \mu(\Theta, t) e^{j\Theta(\vec{r}) - t/T_2} + D\nabla^2 \mu(\Theta, t) e^{j\Theta(\vec{r}) - t/T_2}. \tag{B.45}
\]
Through simplifying pieces of the equation separately, the answer may be understood better. Starting with the left hand side of the equation,

\[
\frac{\partial \mu(\Theta, t) e^{j \Theta(\vec{r}) - t/T_2}}{\partial t} = \mu(\Theta, t) \frac{\partial e^{j \Theta(\vec{r}) - t/T_2}}{\partial t} + \frac{\partial \mu(\Theta, t)}{\partial t} e^{j \Theta(\vec{r}) - t/T_2}
\]

\[
= \left[ \mu(\Theta, t) \frac{\partial}{\partial t} \left( j \Theta(\vec{r}) - \frac{t}{T_2} \right) + \frac{\partial \mu(\Theta, t)}{\partial t} \right] e^{j \Theta(\vec{r}) - t/T_2}
\]

\[
= \left[ \mu(\Theta, t) \left( -\frac{1}{T_2} \right) + \frac{\partial \mu(\Theta, t)}{\partial t} \right] e^{j \Theta(\vec{r}) - t/T_2}. \tag{B.46}
\]

Moving to the Laplacian, solving for the partial derivatives of \(x\) first

\[
\frac{\partial^2 \mu(\Theta, t) e^{j \Theta(\vec{r}) - t/T_2}}{\partial x^2} = \frac{\partial}{\partial x} \left( \frac{\partial \mu(\Theta, t) \partial \Theta}{\partial x} + j \mu(\Theta, t) \frac{\partial \Theta(\vec{r})}{\partial x} \right) e^{j \Theta - t/T_2}
\]

\[
= \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} \left( \frac{\partial \Theta}{\partial x} \right)^2 + j \frac{\partial \mu(\Theta, t)}{\partial \Theta} \left( \frac{\partial \Theta}{\partial x} \right)^2 \right.
\]

\[
+ \left. j \frac{\partial \Theta}{\partial x} \left[ \frac{\partial \mu(\Theta, t) \partial \Theta}{\partial x} + j \mu(\Theta, t) \frac{\partial \Theta}{\partial x} \right] \right) e^{j \Theta(\vec{r}) - t/T_2}
\]

\[
= \left( \frac{\partial \Theta}{\partial x} \right)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} - \mu(\Theta, t) \right) e^{j \Theta(\vec{r}) - t/T_2}
\]

\[
= (\gamma G_x \tau)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} - \mu(\Theta, t) \right) e^{j \Theta(\vec{r}) - t/T_2}, \tag{B.47}
\]

where (B.8) and (B.9) are used as before. Again, following the same process as (B.47)

\[
\frac{\partial^2 \mu(\Theta, t) e^{j \Theta(\vec{r}) - t/T_2}}{\partial y^2} = (\gamma G_y \tau)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} - \mu(\Theta, t) \right) e^{j \Theta(\vec{r}) - t/T_2}, \tag{B.48}
\]

and

\[
\frac{\partial^2 \mu(\Theta, t) e^{j \Theta(\vec{r}) - t/T_2}}{\partial z^2} = (\gamma G_z \tau)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} - \mu(\Theta, t) \right) e^{j \Theta(\vec{r}) - t/T_2}. \tag{B.49}
\]

Next, substituting into (B.2) it becomes

\[
\nabla^2 \mu(\Theta, t) = (\gamma G \tau)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} - \mu(\Theta, t) \right) e^{j \Theta(\vec{r}) - t/T_2}. \tag{B.50}
\]
Finally, using the pieces from (B.44) (B.46) and (B.50), (B.1) for the time period after the gradient pulse is

\[
\frac{\partial \mu(\Theta, t)}{\partial t} e^{j\Theta(t) - t/T_2} = D (\gamma G r)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} - \mu(\Theta, t) \right) e^{j\Theta(t) - t/T_2}.
\]

(B.51)

\[
\frac{\partial \mu(\Theta, t)}{\partial t} = D (\gamma G r)^2 \left( \frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} + 2j \frac{\partial \mu(\Theta, t)}{\partial \Theta} - \mu(\Theta, t) \right).
\]

Solution as a Fourier Integral: Now that (B.1) is simplified into (B.51) for the first time period, the solution may be represented as a Fourier integral of the form

\[
\mu(\Theta, t) = \int_{-\infty}^{+\infty} a''(k) e^{A''} e^{j\Theta} dk,
\]

(B.52)

where \(a''(k)\) and \(A''\) are unknown functions, as before. Equation (B.52) may be substituted into (B.51) to solve for one of those unknowns, \(A''\). Approaching the left and right hand sides of (B.51) one at a time will provide a derivation that is more clear. Starting with the left hand side,

\[
\frac{\partial \mu(\Theta, t)}{\partial t} = \int_{-\infty}^{+\infty} a''(k) e^{A''} \frac{\partial A''}{\partial t} e^{j\Theta} dk,
\]

(B.53)

where all time dependence is again assumed to be in \(A''\). Moving on to the right hand side, starting with the single derivative

\[
\frac{\partial \mu(\Theta, t)}{\partial \Theta} = \int_{-\infty}^{+\infty} a''(k) e^{A''} e^{j\Theta} jk dk.
\]

(B.54)

Then, moving to the second derivative

\[
\frac{\partial^2 \mu(\Theta, t)}{\partial \Theta^2} = -\int_{-\infty}^{+\infty} a''(k) e^{A''} e^{j\Theta} k^2 dk.
\]

(B.55)
Next, substituting (B.52), (B.53), (B.54), and (B.55) into (B.51) it becomes

\[ \int_{-\infty}^{+\infty} a''(k)e^{A''}\frac{\partial A''}{\partial t} e^{j\Theta} dk = D (\gamma G \tau)^2 \left( - \int_{-\infty}^{+\infty} a''(k)e^{A''} e^{j\Theta} k^2 dk + 2j \int_{-\infty}^{+\infty} a''(k)e^{A''} e^{j\Theta} jk dk - \int_{-\infty}^{+\infty} a''(k)e^{A''} e^{j\Theta} dk \right) \]

\[ \int_{-\infty}^{+\infty} a''(k)e^{A''}\frac{\partial A''}{\partial t} e^{j\Theta} dk = - \int_{-\infty}^{+\infty} D (\gamma G \tau)^2 a''(k)e^{A''} (k^2 + 2k + 1) e^{j\Theta} dk \]

\[ 0 = \int_{-\infty}^{+\infty} a''(k)e^{A''} \times \left[ \frac{\partial A''}{\partial t} + D (\gamma G \tau)^2 (k^2 + 2k + 1) \right] e^{j\Theta} dk. \]

This requirement may be satisfied with

\[ 0 = \frac{\partial A''}{\partial t} + D (\gamma G \tau)^2 (k + 1)^2 \]

\[ \frac{\partial A''}{\partial t} = -D (\gamma G \tau)^2 (k + 1)^2 \]

\[ A'' = -D (\gamma G \tau)^2 (k + 1)^2 t. \]

**B.2 Continuity of Magnetization**

So far, we have solved the transverse magnetization for the three different time periods. Imposing continuity across time periods allows us to relate these expressions to one another.

I will start with the continuity between the first two time periods by equating (B.4) and (B.27) at the boundary time of \( \epsilon \),

\[ M^+ (\Theta, \epsilon^-) = M^+ (\Theta, \epsilon^+) \]

\[ \mu (\Theta, \epsilon^-) e^{-\epsilon^-/T_2} = \mu (\Theta, \epsilon^+) e^{\epsilon^+/(\tau - \epsilon^-)/T_2} \]

\[ \mu (\Theta, \epsilon^-) = \mu (\Theta, \epsilon^+). \]

Next, using (B.26) substituted into (B.22) and (B.43) substituted into (B.36), (B.58) becomes

\[ \int_{-\infty}^{+\infty} a(k)e^{-D(\gamma G \tau)^2 k^2 \epsilon} e^{j\Theta} dk = \int_{-\infty}^{+\infty} a'(k)e^{-\frac{\epsilon}{2}D(\gamma G \tau)^2 (k + \frac{\epsilon}{2})^3} e^{j\Theta} dk \]

\[ = \int_{-\infty}^{+\infty} a'(k)e^{-\frac{\epsilon}{2}D(\gamma G \tau)^2 k^3} e^{j\Theta} dk. \]
By invoking the orthogonality of \( \exp(jk\Theta) \) in (B.59), the equality becomes

\[
\begin{align*}
    a(k)e^{-D(\gamma G\tau)^2k^2} &= a'(k)e^{-\frac{j}{2}D(\gamma G\tau)^2k^3} \\
    a(k)e^{-D(\gamma G\tau)^2k^2}e^{\frac{j}{2}D(\gamma G\tau)^2k^3} &= a'(k) \\
    a(k)e^{-D(\gamma G\tau)^2k^2(\epsilon - \frac{k^2}{2})} &= a'(k).
\end{align*}
\] (B.60)

Moving on to the second and third time periods by equating (B.27) and (B.44) at the boundary time of \( \epsilon + \tau \),

\[
M^+(\Theta, \epsilon + \tau^-) = M^+(\Theta, \epsilon + \tau^+) = \mu(\Theta, \epsilon + \tau^-) e^{j(\epsilon + \tau^-)/\tau - (\epsilon + \tau^+)/T_2} = \mu(\Theta, \epsilon + \tau^+) e^{j(\epsilon + \tau^+)/T_2}
\] (B.61)

Then, similar to above, using (B.43) substituted into (B.36) and (B.57) substituted into (B.52), (B.61) becomes

\[
\begin{align*}
    \int_{-\infty}^{+\infty} a'(k)e^{-\frac{j}{2}D(\gamma G\tau)^2(k+\frac{\epsilon+\tau}{\tau})^3} e^{jk\Theta} dk = \int_{-\infty}^{+\infty} a''(k)e^{-D(\gamma G\tau)^2(k+1)^2(\tau+\epsilon)} e^{jk\Theta} dk \\
    \int_{-\infty}^{+\infty} a'(k)e^{-\frac{j}{2}D(\gamma G\tau)^2(k+1)^3} e^{jk\Theta} dk = \int_{-\infty}^{+\infty} a''(k)e^{-D(\gamma G\tau)^2(k+1)^2(\tau+\epsilon)} e^{jk\Theta} dk.
\end{align*}
\] (B.62)

Again invoking the orthogonality of \( \exp(jk\Theta) \) in (B.62), the equality becomes

\[
\begin{align*}
    a'(k)e^{-\frac{j}{2}D(\gamma G\tau)^2(k+1)^3} &= a''(k)e^{-D(\gamma G\tau)^2(k+1)^2(\tau+\epsilon)} \\
    a'(k) &= a''(k)e^{-D(\gamma G\tau)^2(k+1)^2(\tau+\epsilon)} e^{\frac{j}{2}D(\gamma G\tau)^2(k+1)^3} \\
    a'(k) &= a''(k)e^{-D(\gamma G\tau)^2(k+1)^2[\tau+\epsilon - \frac{k^2}{2}]} \\
    a'(k) &= a''(k)e^{-D(\gamma G\tau)^2(k^2+2k+1)(\frac{2}{3}\tau+\epsilon - \frac{k^2}{2})}.
\end{align*}
\] (B.63)

Then, substituting (B.60) into (B.63)

\[
\begin{align*}
    a(k)e^{-D(\gamma G\tau)^2k^2(\epsilon - \frac{k^2}{2})} &= a''(k)e^{-D(\gamma G\tau)^2(k^2+2k+1)(\frac{2}{3}\tau+\epsilon - \frac{k^2}{2})} \\
    a(k) &= a''(k)e^{-D(\gamma G\tau)^2(k^2+2k+1)(\frac{2}{3}\tau+\epsilon - \frac{k^2}{2})} e^{D(\gamma G\tau)^2k^2(\epsilon - \frac{k^2}{2})} \\
    a(k) &= a''(k)e^{-D(\gamma G\tau)^2[(k^2+2k+1)(\frac{2}{3}\tau+\epsilon - \frac{k^2}{2})-k^2(\epsilon - \frac{k^2}{2})]} \\
    a(k)e^{D(\gamma G\tau)^2[\epsilon(\frac{2}{3}\tau+\epsilon)+\epsilon(2k+1)]} &= a''(k).
\end{align*}
\] (B.64)

### B.3 Longitudinal Magnetization Solution

A solution may be obtained for the longitudinal magnetization by following a similar method to the transverse magnetization. The Bloch-Torrey equation for longitudinal magnetization is

\[
\frac{\partial M_z}{\partial t} = \frac{M_0 - M_z}{T_1} + D\nabla^2 M_z.
\] (B.65)
The longitudinal magnetization may be represented as
\[ M_z(\Theta, t) = M_0 + \nu(\Theta, t)e^{-t/T_1}. \] (B.66)

I will prepare to combine these equations by solving for individual pieces of (B.65) at a time. First, the time derivative
\[ \frac{\partial M_z}{\partial t} = \frac{\partial M_0 + \nu(\Theta, t)e^{-t/T_1}}{\partial t} = \left( -\frac{1}{T_1} \right) \nu(\Theta, t)e^{-t/T_1} + \frac{\partial \nu(\Theta, t)}{\partial t}e^{-t/T_1}. \] (B.67)

Following that with the Laplacian, starting with the partial derivative of x
\[ \frac{\partial^2 M_z}{\partial x^2} = \frac{\partial^2 M_0 + \nu(\Theta, t)e^{-t/T_1}}{\partial x^2} = \frac{\partial}{\partial x} \left( \frac{\partial \nu(\Theta, t)}{\partial \Theta} \frac{\partial \Theta}{\partial x} \right) e^{-t/T_1} = \left( \frac{\partial}{\partial x} \left( \frac{\partial \nu(\Theta, t)}{\partial \Theta} \frac{\partial \Theta}{\partial x} \right) \right) e^{-t/T_1} = \frac{\partial^2 \nu(\Theta, t)}{\partial \Theta^2} \left( \frac{\partial \Theta}{\partial x} \right)^2 e^{-t/T_1}. \] (B.68)

Partial derivatives with respect to y and z will yield similar results with the Laplacian being
\[ \nabla^2 = \frac{\partial^2 \nu(\Theta, t)}{\partial \Theta^2} (\gamma G \tau)^2 e^{-t/T_1}. \] (B.69)

Therefore, equation (B.65) is
\[ \left( -\frac{\nu(\Theta, t)}{T_1} + \frac{\partial \nu(\Theta, t)}{\partial t} \right) e^{-t/T_1} = \left( M_0 - M_0 - \nu(\Theta, t) \right) + D \frac{\partial^2 \nu(\Theta, t)}{\partial \Theta^2} (\gamma G \tau)^2 e^{-t/T_1} \] (B.70)
\[ \frac{\partial \nu(\Theta, t)}{\partial t} = D \frac{\partial^2 \nu(\Theta, t)}{\partial \Theta^2} (\gamma G \tau)^2. \]

Where (B.70) is of the same form as (B.21), therefore the Fourier solution will take the same form as (B.22),
\[ \nu(\Theta, t) = \int_{-\infty}^{+\infty} c(k)e^{C}e^{ik\Theta}dk \] (B.71)

where
\[ C = -D(\gamma G \tau)^2k^2t. \] (B.72)