Improved Accuracy in Susceptibility-based OEF Measurements
by Mitigation of Partial-Volume Effects via Combined Magnitude
and Phase Reconstruction

by Patrick C. McDaniel

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ABSTRACT

Regional quantitative Oxygen Extraction Fraction (OEF) values can only be reliably obtained from blood vessels larger than the acquisition voxel size. Blood vessels beyond this limit produce unreliable measurements due to partial-volume effects. We demonstrate a method for obtaining more reliable OEF measurements beyond this limit by performing a joint reconstruction using both the magnitude and phase of the complex-valued MRI signal. This method is validated both in numerical simulations and on in vivo data.

The ability to perform high-quality fetal brain imaging is hampered by motion of the fetus, which can severely degrade image quality. Previously, low-resolution volumetric navigator (vNav) acquisitions have been shown to accurately track motion in human adults and prospectively correct for it. Here, a technique for using vNavs to measure fetal head motion in utero is developed and validated on in vivo data.

Parallel Transmission (pTx) improves image quality and patient safety in high-field MRI. Unlike in single-channel MR excitation, an array of multiple excitation coils is used in pTx. However, coupling between these independent coils significantly degrades the power efficiency of the pTx array. Previously, it a decoupling matrix was proposed to solve this inefficiency. In this work, a physical realization of a 4-channel decoupling matrix was constructed and tested.

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Chapter 1
Improved Estimation of Oxygen Extraction Fraction (OEF) Using MRI via Joint Utilization of Magnitude and Phase (JUMP) Reconstruction

Part 1: Introduction

Summary
Susceptibility-Weighted Imaging (SWI) is a method of magnetic resonance imaging (MRI) that generates images with contrast between structures that is not seen in other modalities. In addition to several clinical uses, it also serves as a robust technique for obtaining in vivo local blood oxygenation measurements. Herein is described a novel method for improving these blood oxygenation measurements obtained via SWI.

SWI and Clinical Uses

Clinical SWI
Susceptibility-Weighted Imaging (SWI) is an MR technique that exploits physiological susceptibility variations within tissue to create image contrast. Examples of such physiological susceptibility variations are: iron deposits, white matter tracts, and deoxyhemoglobin in venous vasculature [SMittal2009]. In particular, the sensitivity of SWI to deoxygenated blood has led to many clinical applications, including: superior detection of small hemorrhagic lesions and detection of underperfused tissue in cases of stroke [KATong2004].

Need for Quantitative Susceptibility-Based Imaging
While qualitative clinical SW images have diagnostic value, the mathematical relationship between blood oxygen saturation (SvO2) and susceptibility means that quantitative SWI can provide quantitative measurements of blood oxygen saturation. Several methods for making such measurements and several applications for them have been reported.

Large Vessel (Global) Venography
The Superior Sagittal Sinus is a large venous sinus that accounts for around 47% of the venous drainage of the entire vein. This fraction can be easily measured and has been shown to be robust to apneic challenge conditions, suggesting that OEF measurements in the Superior Sagittal Sinus are a good proxy for global cerebral OEF values [ZRodgers2013]. Additionally, the Superior Sagittal Sinus is vertically-oriented for much of its length, making it a good candidate for MR susceptometry by direct measurement of phase [VJain2010]. Both [ZRodgers2013] and [VJain2010] used MR GRE phase measurements in the Superior Sagittal Sinus to measure venous oxygen saturation (SvO2) as a part of a
reliable method for quantifying CMRO$_2$. Their studies simultaneously acquired velocity-encoded phase-contrast information and susceptibility-based phase information from the same signal, allowing them to obtain high-temporal resolution measurements of total cerebral blood flow (CBF) and OEF. However, their methods only enabled them to obtain average measurements of these physiologic quantities for the whole brain.

**Small Vessel (Local) Venography**

While global measurements of OEF and CMRO$_2$ are clinically valuable, there is further need for localized measurements of OEF. Regional measurements of OEF can be used to assess tumor hypoxia, which is known to confound the effects of certain cancer treatments. Additionally, therapies exist that specifically target hypoxic tissue, making local OEF measurements a clinically useful tool \cite{SDavda2006}.

Direct OEF measurement from vertical veins has been used to assess effects of stroke \cite{MLi2013}, to measure OEF in the spinal vein \cite{NFujima2011}, to measure OEF in patients with multiple sclerosis \cite{APFan2015}, to measure OEF for calculating regional CMRO$_2$ \cite{APFan2012}, and to assess differences in OEF due to sedation \cite{JGoodwin2014}.

Several of these papers specifically mention finite image resolution and partial-volume effects as limiting the accuracy of their results \cite{MLi2013, JGoodwin2014}.

**Significance of this Work and Precedent in Other Studies**

**Significance of this Work**

The method described here utilizes the quantitative values of both the magnitude and phase from the complex-valued MR signal to obtain more accurate OEF measurements. This is done by modeling the partial-voluming behavior within the voxel and its subsequent effect on voxel signal to estimate both the degree of partial-voluming and the susceptibility of the region in question. There are several advantages and innovations of this method:

- **Measurements of SvO$_2$ in Smaller Vessels**: Structures that can be visually resolved in an image, but which are smaller than the acquisition voxel size, do not give accurate SvO$_2$ measurements using traditional techniques and must be excluded from quantitative analysis. With this method, such vessels can yield accurate quantitative analysis.

- **More Data Points per Vessel**: Previously, only voxels that entirely consisted of tissue from the vein being measured could be used, as they were the only ones which did not suffer from partial-volume effects. This effectively limits the number of susceptibility measurements that can be made, yielding greater uncertainty in the estimated SvO$_2$ values. With this method, voxels that occur on the edges of venous structures and suffer from partial volume effects still yield useful measurements, effectively allowing for more data points and less measurement uncertainty.

- **Applicability to Other Modalities**: The premise of this model is that there is, within voxels, underlying phase variation. The model’s assumptions are not specific to SWI, and this model could be applied to Phase-Contrast MRI, TRUST-MRI, BOLD fMRI, spectroscopic MRI, or any other method
for which this premise is true. To our knowledge, this is the first example of using in a quantitative way both components of the complex-valued MR signal.

**Use of Magnitude and Phase Images in Image Reconstruction/Analysis**

Previous MR susceptometry studies have made use of GRE magnitude in addition to GRE phase to improve reconstructed susceptibility measurements. The reconstruction of the susceptibility map $\chi(\vec{r})$ from the phase map $\Delta \varphi(\vec{r})$ is complicated by the zeros in the dipole kernel $\vec{D}(\vec{K})$ at certain values of $\vec{K}$:

$$\vec{D}(\vec{K}) = B_0 \left( \frac{1}{3} - \frac{k_z^2}{k_x^2 + k_y^2 + k_z^2} \right)$$

Since we know that:

$$\Delta \varphi(\vec{r}) = \gamma \cdot \Delta B(\vec{r}) \cdot TE$$

Taking the Fourier Transform:

$$\Delta \vec{\varphi}(\vec{K}) = \gamma \cdot TE \cdot \vec{D}(\vec{K}) \cdot \vec{\chi}(\vec{K})$$

This means a measurement of phase $\Delta \vec{\varphi}(\vec{K})$ is equivalent to an undersampled version of the true susceptibility $\vec{\chi}(\vec{K})$, with $\vec{D}(\vec{K})$ serving as the undersampling mask. In order to reconstruct $\vec{\chi}(\vec{K})$ accurately, one must use additional information.

One approach is to impose regularization on the reconstructed susceptibility map. This helps to reconstruct the underdetermined problem of $\vec{\chi}(\vec{K})$ reconstruction by forcing the image-domain solution $\hat{\chi}(\vec{r})$ to have a minimum of edges. This is a logical constraint to impose, since it is observed that tissue parameters (T1, T2, $\chi$, etc.) do not change much voxel-by-voxel except when changing from one tissue class region to another (eg when going from gray matter to venous blood).

As an alternative, Liu et al. reconstructed $\hat{\chi}(\vec{r})$ from $\Delta \varphi(\vec{r})$ using additional information from the magnitude image of the same GRE acquisition used to measure $\Delta \varphi(\vec{r})$ (JLiu2012). Instead of using the reconstructed $\hat{\chi}$-map for their regularization, they used the simultaneously-acquired GRE magnitude as structural prior to estimate the location of edges in $\vec{\chi}$.

**Use of Magnitude and Phase Images in Clinical SWI**

Clinical susceptibility-weighted imaging (SWI) makes use of both the magnitude and phase images of GRE acquisition to create a single composite image with maximum susceptibility-based contrast [EMHaacke2009]. This image is more accessible to radiologists than the uncombined magnitude and phase images and used in clinical diagnostics as “an adjunct to […] conventional spin density, T1- and T2-weighted imaging methods.” [EMHaacke2009p19]

The manner in which magnitude and phase are combined in SWI specifically accounts for partial-volume effects that occur at the interface between regions of different susceptibility. Voxels that are located at such boundaries contain tissues with different susceptibilities and thus, different $\Delta B_0$ offsets. Therefore,
different regions of these voxels will accrue signal phase at different rates, leading to intra-voxel dephasing and $T_2'$ decay in the magnitude of the GRE signal. These voxels appear dark on the GRE magnitude image.

Voxels that contain only tissue of a single susceptibility do not show this $T_2'$ decay in the magnitude image, even if the susceptibility is different from the “background susceptibility.” However, this different susceptibility is precisely what we want to be a source of image contrast. This problem is solved by using the phase of the GRE acquisition. In regions of uniform, non-background susceptibility, the signal will have some non-zero phase. However, the phase image by itself contains many artifacts in addition to the physiological tissue phase, and is unsuitable by itself for clinical use.

Instead, the phase image is used to create a mask that is then applied to the magnitude image. On this composite image, regions of high phase and regions of high $T_2'$ decay will both appear dark. This maximizes the image contrast that originates in susceptibility variations within the brain.

**Modeling of Partial-Volume Effects in the Other MR Modalities**

**BOLD**: Prior studies of the Blood Oxygen Level-Dependent (BOLD) effect have modeled the effects of partial-voluming within a voxel on that voxel’s signal evolution. In one study, it was observed in simulations that partial-volume effects between veins and Gray Matter parnechyma contribute significantly to both BOLD GRE and SE contrast [JMZhao2007]. This study incorporated a forward model by using, a priori knowledge of $T2^*$, $T2$, $T1$, water fraction of tissue, and tissue fractions for gray matter and observing the effects of these parameters on voxel signal values.

**DTI**: Partial-volume effects are significant in Diffusion Tensor Imaging (DTI). In DTI, diffusion of water molecules leads to the dephasing of magnetization vectors in the final signal, resulting in attenuation in regions with high diffusivity. This dephasing occurs because of how gradient fields are played. In general, local diffusivity might be higher along one axis than another: eg in a white matter tract, water is more likely to diffusion along the direction of the fiber than to diffuse across the cell wall. In this general case, diffusivity is not described by a scalar value, but by a symmetric 3x3 diffusion tensor [DLeBihan2001].

Implicit in DTI is that each voxel is described by a single diffusion tensor. In situations where a voxel contains multiple regions, with each described by a different diffusion tensor, this assumption is invalid and the resulting measurement will be less meaningful. It has been shown that partial-volume effects in DTI can lead to significant errors in diffusion tensor measurement, particularly in cases of little inter-compartment exchange and diffusion anisotropy [ALAlexander2001].

**Fat/Water Separation in Spectroscopic Imaging**

Differing resonance frequencies due to chemical shift also cause intravoxel signal dephasing in MR imaging. One case of this is the fat-water frequency shift, where protons in fat precess at a lower frequency than protons in water. At 3T, this frequency difference, $\Delta f$, is approximately 430Hz. A voxel may contain both fat and water molecules, and thus contain regions of signal precessing at both frequencies. The phase difference between these two signals at a given echo time (TE) is:
If $\Delta \varphi = \pi$, then the two signals will be out of phase. When this occurs, they will destructively add. However, when $\Delta \varphi = 2\pi$, the signals will be in phase, and will constructively add.

In effect, the signal in the first case will be the difference between the water signal and the fat signal. Likewise, the second case will yield the sum of the water signal and the fat signal. By taking the sum and difference of the two acquired signals, one can reconstruct a “water” signal, and a “fat” signal, respectively [WTDixon1984]. The same vector-dephasing model is employed here as in prior spectroscopic imaging studies based on this phenomenon [WTDixon1984]. Here, however, we treat both image magnitude and phase quantitatively in order to infer sub-voxel tissue information.
**Part 2: Theory**

**Summary**

The magnetic susceptibility of blood varies linearly with its oxygen saturation. Such susceptibility variations within the brain cause variations in local magnetic field. By knowing the effects of these magnetic field variations on the acquired MR signal, we can use magnitude and phase signal values to estimate those same susceptibility variations, and ultimately, local blood oxygenation status.

When a single voxel contains multiple tissue types, each with different magnitude intensity and phase, partial-volume effects occur. In this case, the measured magnitude and phase do not provide meaningful information about the susceptibility of either tissue. However, by modeling how partial-volume effects manifest themselves and understanding the tissues being mixed, it is possible to make accurate measurements of tissue susceptibility.

We propose a method called Joint Utilization of Magnitude and Phase (JUMP) that reliably estimates OEF from blood vessels that suffer from partial-volume effects [PMcDaniel2015].

**Effect of Blood Oxygenation on Magnetic Susceptibility**

**Definition of Magnetic Susceptibility**

Susceptibility ($\chi$) is defined in equation (1) as the relation between magnetic field and magnetization in a particular material.

$$ \vec{M} = \chi \cdot \frac{\vec{B}}{\mu_0} \quad (1) $$

In the most general case, $\chi$ is a second-rank tensor and is expressed as a Hermitian 3x3 matrix (six unique elements). Some studies have exploited this fact to measure directional anisotropies in susceptibility within the brain [CLiu2010] but we will assume $\chi$ is a scalar quantity.

*Paramagnetic* materials are those for which susceptibility is positive, and *diamagnetic* materials are those for which it is negative. Diamagnetism results from the behavior of atoms’ orbiting electrons in the presence of the magnetic field. When placed in a constant magnetic field $\vec{B}$, the electrons’ motion is perturbed. The perturbation is equivalent to an induced magnetization that is antiparallel to $\vec{B}$, making $\chi$ negative. [HEssén1989] All materials exhibit this phenomenon to some degree. Water, and thus water-containing tissues, are overall diamagnetic relative to free space.

In paramagnetic materials however, the diamagnetism of the orbiting electrons is cancelled out by the presence of unpaired electrons and their intrinsic magnetic moments. When placed in a magnetic field, these moments tend to align parallel with it, making $\chi$ positive. For example, an oxygen molecule contains 2 unpaired electrons, making oxygen paramagnetic. The paramagnetic behavior of the
electrons’ intrinsic spins dominates the diamagnetic behavior of their orbits, giving such materials overall positive susceptibility.

Relative to free space, blood – even when fully deoxygenated – is diamagnetic. However, relative to water, it is paramagnetic. This difference – not that relative to vacuum – is what’s of interest in MRI. Thus, all subsequent definitions of susceptibility or susceptibility difference will be implicitly measured relative to the susceptibility of water.

Hemoglobin

The hemoglobin molecule is the means by which oxygen is transported to cells so they may perform oxidative respiration. A hemoglobin molecule consists of 4 heme groups, each of which contains a ferrous iron atom (Fe$^{2+}$) to which an oxygen molecule can bind. The oxygen saturation (SvO$_2$ for veins, SaO$_2$ for arteries) of blood is the fraction of these oxygen binding sites that are bound to oxygen molecules (O$_2$).

If no O$_2$ is bound to the iron atom, its electron configuration contains 4 unpaired electrons due to a 5-fold degeneracy in the highest-energy occupied electron orbitals. This makes the atom strongly paramagnetic. When O$_2$ binds to the iron atom, the 5 previously degenerate orbitals split into 3 lower-energy and 2 higher-energy orbitals. The iron atom’s 6 electrons fill the 3 low-energy orbitals, so that then all electrons are paired the atom is no longer paramagnetic. [YWang2014]

Blood with lower oxygen saturation has more unbound iron atoms, and is therefore more paramagnetic. The susceptibility of blood is linearly proportional to the number of unbound iron atoms it contains, meaning it depends on both the quantity of hemoglobin and the fraction of O$_2$ sites that are unbound:

$$\chi_b \sim Hct \times (1 - SvO_2)$$

Hct stands for hematocrit, the fraction of blood composed of red blood cells. The proportionality factor is the susceptibility of fully-deoxygenated red blood cells, $\chi_{do}$:

$$\chi_b = \chi_{do} \times Hct \times (1 - SvO_2) \quad (2)$$

The value of $\chi_{do}$ is approximately 0.27 ppm in CGS units ($4\pi \times 0.27 \text{ ppm} = 3.39 \text{ ppm}$ in SI units). [VJain2012] We will treat this value as a constant, as the fraction of red blood cells that consists of hemoglobin varies little from person to person. (RBC HEMOGLOBIN FRACTION CITATION) Using equation (2), we can now easily calculate SvO$_2$ from a measurement of blood susceptibility $\chi_b$.

Susceptibility Effects on Magnetic Field

Susceptibility in Classical Electromagnetic Theory
Scalar magnetic susceptibility ($\chi$) can be defined as the ratio of the magnetization ($M$, magnetic dipole per unit volume) induced in a material to the magnetizing field ($\frac{B}{\mu_0}$). In general, each quantity can vary with position. Recall equation (1):

$$\vec{M}(\vec{r}) = \chi(\vec{r}) \cdot \vec{B}(\vec{r}) \frac{1}{\mu_0}$$

This induced magnetic dipole per unit volume in turn generates its own dipole magnetic field. For a magnetized volume $dV$ located at $\vec{r}'$, the dipole field generated at $\vec{r}$ (call it $d\vec{B}_{\text{ind}}(\vec{r}, \vec{r}')$), in terms of induced magnetic dipole per unit volume ($\vec{M}(\vec{r}')$) is, from [DKCheng1989]:

$$d\vec{B}_{\text{ind}}(\vec{r}, \vec{r}') = \frac{\mu_0(dV \cdot |\vec{M}(\vec{r}')|)}{4\pi |\vec{r} - \vec{r}'|^3} \left(2 \cos(\theta) \hat{r} + \sin(\theta) \hat{\theta} \right)$$

$$= \frac{\mu_0}{4\pi} \frac{3dV |\vec{M}(\vec{r}')|}{|\vec{r} - \vec{r}'|^5} \left(\frac{(\vec{r} - \vec{r}') \cdot (\vec{r} - \vec{r}')}{|\vec{r} - \vec{r}'|^3} - \frac{\vec{M}(\vec{r}')}{|\vec{r} - \vec{r}'|^3}\right)$$

The induced magnetic field is a three-dimensional vector, but components of this field perpendicular to $B_0$ (z-axis) do not affect the MR signal. Also, since $B_0$ is oriented along the z-axis, $\vec{M}$ is also oriented along the z-axis (from (1)). We are then only interested in the z-component of $d\vec{B}_{\text{ind}}$:

$$dB_{z,\text{ind}}(\vec{r}, \vec{r}') = d\vec{B}_{\text{ind}}(\vec{r}, \vec{r}') \cdot \vec{M}$$

$$= \frac{\mu_0(dV \cdot |\vec{M}(\vec{r}')|)}{4\pi |\vec{r} - \vec{r}'|^3} (3\cos^2(\theta) - 1) \quad (3)$$

In the case of MRI, the magnetic field is oriented along $\hat{z}$ and has a magnitude $B_0$. Assuming a point susceptibility source at the origin, and combining equations (1) and (3):

$$dB_{z,\text{ind}}(\vec{r}, \vec{r}') = dV \frac{B_0 \chi(\vec{r}')}{{4\pi |\vec{r} - \vec{r}'|^3}} (3\cos^2(\theta) - 1)$$

$$= dV \frac{B_0 \chi(\vec{r}')}{{4\pi |\vec{r} - \vec{r}'|^3}} \left(3 \frac{[(\vec{r} - \vec{r}') \cdot \hat{z}]^2}{|\vec{r} - \vec{r}'|^2} - 1 \right)$$

The total susceptibility-induced magnetic field is the integral of this quantity over all susceptibility variations in space:

$$B_{z,\text{ind}}(\vec{r}) = \int d^3 \vec{r}' \frac{B_0 \chi(\vec{r}')}{{4\pi |\vec{r} - \vec{r}'|^3}} \left(3 \frac{[(\vec{r} - \vec{r}') \cdot \hat{z}]^2}{|\vec{r} - \vec{r}'|^2} - 1 \right)$$

This is mathematically equivalent to the convolution of the susceptibility distribution $\chi(\vec{r})$ with an impulse response $d(\vec{r})$, where $d(\vec{r})$ is the dipole kernel and is given in spherical coordinates by:
\[ d(\bar{r}) = \frac{B_0}{4\pi r^3} (3\cos^2(\theta) - 1) \]

Then, we have:

\[ B_{z,ind}(\bar{r}) = (\chi \ast d)(\bar{r}) \]

**Fourier Domain Representation**

We can also write the previous equation in the Fourier Domain by evaluating the Fourier Transform of \( d(\bar{r}) \), \( \tilde{D}(\mathbf{k}) \):

\[ \tilde{D}(\mathbf{k}) = \int d^3r \frac{B_0}{4\pi r^3} (3\cos^2(\theta) - 1) e^{i(\mathbf{k}\cdot\bar{r})} \quad (4) \]

This integral can be evaluated in spherical coordinates by following the derivation in [JPMarques2005]. First, the quantity \( \mathbf{k} \cdot \bar{r} \) can be expressed as \( |\mathbf{k}| |\bar{r}| \cos(\alpha) = k \cdot r \cdot \cos(\alpha) \). Here, \( \alpha \) is a variable to integrated over, and is the angle between \( \mathbf{k} \) and \( \bar{r} \). With respect to the integral, \( \mathbf{k} \) is fixed.

The angle \( \theta \) is the polar angle between \( \bar{r} \) and the z-axis and is a variable to be integrated over. In order to evaluate the integral, we need to re-write \( \theta \) in terms of \( \alpha \). This is shown in Figure 1.1. In this figure, the coordinate system is aligned with \( \hat{\mathbf{k}} \), which is fixed with respect to the integral. The vector \( \hat{\mathbf{z}} \) is also fixed, and only serves as the axis used to measure the angle \( \theta \). The angle \( \alpha \), as defined above, is shown to be the angle between \( \mathbf{k} \) and \( \bar{r} \). \( \phi \) is the azimuthal angle which specifies \( \bar{r} \) in the new \( \hat{\mathbf{k}} \)-based coordinates.

In Figure 1.1, the length \( l \) is first found in terms of \( \phi, \alpha, \) and \( \beta \). Knowing \( l \) enables the calculation of \( \theta \):

\[ \cos(\theta) = \cos(\alpha) \cos(\beta) + \sin(\alpha) \sin(\beta) \cos(\phi) \]

If we plug this into Equation (4), we get:

\[
\tilde{D}(\mathbf{k}) = \int dr \int d\alpha \int_0^{2\pi} \left[ r \sin(\alpha) d\phi \frac{B_0}{4\pi r^3} e^{i(k \cdot r \cdot \cos(\alpha))} (3[\cos^2(\alpha)\cos^2(\beta) + \sin^2(\alpha)\sin^2(\beta)\cos^2(\phi) + 2 \cos(\alpha) \cos(\beta) \sin(\alpha) \sin(\beta) \cos(\phi)] - 1) \right]
\]

Integrating over \( \phi \) is easy, and gives:

\[ \tilde{D}(\mathbf{k}) = 2\pi \int dr \int d\alpha sin(\alpha) \left[ \frac{B_0}{4\pi r} e^{i(k \cdot r \cdot \cos(\alpha))} \left( 3[\cos^2(\alpha)\cos^2(\beta) + \frac{1}{2} \sin^2(\alpha)\sin^2(\beta)] - 1 \right) \right] \]
Using another relation from [JPMarques2005]:

\[ \bar{D}(\mathbf{k}) = 2\pi \int_0^\pi d\alpha \int_0^\pi \frac{d\alpha}{4\pi r} e^{jk\cdot r(\alpha)} \left[ \frac{1}{2} (3\cos^2(\alpha) - 1)(3\cos^2(\beta) - 1) \right] \]

\[ = \frac{B_0 (3\cos^2(\beta) - 1)}{4} \int_0^\pi d\alpha \int_0^\pi \frac{d\alpha}{r} \left[ e^{jk\cdot r(\alpha)} \right] \left[ (3\cos^2(\alpha) - 1) \right] \]

Taking advantage of the fact that \( d\alpha \sin(\alpha) = -d(\cos(\alpha)) \), this is equal to:

\[ \bar{D}(\mathbf{k}) = \frac{B_0 (3\cos^2(\beta) - 1)}{4} \int_0^1 d(\cos(\alpha)) \left[ e^{jk\cdot r(\alpha)} \right] \left[ (3\cos^2(\alpha) - 1) \right] \]

The integral over \( \cos(\alpha) \) is now easy to evaluate. The result is:

\[ \bar{D}(\mathbf{k}) = B_0 (3\cos^2(\beta) - 1) \int_0^\infty \frac{dr}{r} \left[ \frac{\sin(kr)}{kr} + 3 \frac{\cos(kr)}{k^2r^2} - 3 \frac{\sin(kr)}{k^3r^3} \right] \]

This integral cannot be evaluated due to the singularity at the origin. We will instead evaluate it with a positive lower limit of integration, and take the limiting case of that lower limit:

\[ \bar{D}(\mathbf{k}) = \lim_{\epsilon \to 0} \left[ B_0 (3\cos^2(\beta) - 1) \int_0^\infty \frac{dr}{r} \left[ \frac{\sin(kr)}{kr} + 3 \frac{\cos(kr)}{k^2r^2} - 3 \frac{\sin(kr)}{k^3r^3} \right] \right] \]

This may seem like just a mathematical trick, but we could equally arrive at the need for this definition by considering the physics of this system. When using equations (1) and (3) to calculate the magnetic field at a given point, we implicitly assume that the susceptibility map \( \chi(\mathbf{r}) \) is a continuum – that is, we ignore the fact that magnetization, and thus, susceptibility, is localized to individual atoms. For most distances \(|\mathbf{r} - \mathbf{r'}| \) in equation (3), \(|\mathbf{r} - \mathbf{r'}| \) is much greater than the atomic spacing, and the continuum approximation is valid. However, for small distances, we need to consider the effects of these individual dipole moments. Fortunately, for a distribution of aligned dipole moments that is spherically symmetrical about a point, the net magnetic field at that point is zero. This sphere in which we consider each dipole moment individually is called a Spherical Lorentz Cavity [CJDurrant2003]. The approximation of spherical symmetry about each point becomes more exact as the size of the sphere tends to zero. Mathematically, we impose this precisely by taking the limit in equation (5). The limit imposes the physically necessary Lorentz Cavity Correction and, mathematically, removes the singularity.

Evaluating this integral, we have:

\[ \bar{D}(\mathbf{k}) = \lim_{\epsilon \to 0} \left[ B_0 (3\cos^2(\beta) - 1) \int_0^\infty \frac{dr}{r} \left[ \frac{\sin(kr)}{kr} + 3 \frac{\cos(kr)}{k^2r^2} - 3 \frac{\sin(kr)}{k^3r^3} \right] \right] \]
\[
\begin{align*}
&= \lim_{\epsilon \to 0} \left[ B_0 \left( 3 \cos^2(\beta) - 1 \right) \frac{\cos(k\epsilon) - \sin(k\epsilon)}{k^2 e^{k\epsilon}} \right] \\
&= \left[ B_0 \left( 3 \cos^2(\beta) - 1 \right) \left( -\frac{1}{3} \right) \right] \\
&= B_0 \left( \frac{1}{3} - \cos^2(\beta) \right)
\end{align*}
\]

Given the definition of \( \beta \) in Figure 1.1, this is equal to:

\[
\mathcal{D}(\mathbf{k}) = B_0 \left( \frac{1}{3} - \frac{k_z^2}{k_x^2 + k_y^2 + k_z^2} \right)
\]

One last issue is that \( \mathcal{D}(\mathbf{k}) \) is not currently defined at \( \mathbf{k} = 0 \). \( \mathcal{D}(0) \) represents the constant induced magnetic field offset due to a constant offset in susceptibility, and has no bearing on measured differences in magnetic field strength between different points. \( \mathcal{D}(0) \) is often defined to account for bulk susceptibility shifts [JPMarques2005], giving it a value of \( \mathcal{D}(0) = \frac{1}{3} \).

Finally, we have the relation between susceptibility and induced magnetic field, in the Fourier Domain:

\[
\mathcal{B}_{z,\text{ind}}(\mathbf{k}) = \mathcal{D}(\mathbf{k}) \cdot \chi(\mathbf{k})
\]

\[
\mathcal{D}(\mathbf{k}) = \begin{cases} 
\frac{1}{3} & \text{if } \mathbf{k} = 0 \\
B_0 \left( \frac{1}{3} - \frac{k_z^2}{k_x^2 + k_y^2 + k_z^2} \right) & \text{otherwise}
\end{cases}
\]

A Note on the Higher-Order Relation between Susceptibility and Magnetization

In general, this induced magnetic field will itself induce further magnetization, which will in turn create additional magnetic field. This can be corrected by modifying equation (1), which becomes:

\[
\mathbf{M}(\mathbf{r}) = \frac{\chi(\mathbf{r})}{1 + \chi(\mathbf{r})} \cdot \frac{\mathbf{B}(\mathbf{r})}{\mu_0}
\]

In our case, however, susceptibilities are small (\( \chi \sim 10^{-6} \)) and this equation reduces to the standard form of equation (1). We can ignore the second- and higher-order terms in \( \chi \) that this correction adds [JNeelavalli2011].

**Susceptibility-Induced Field Variations for Cylindrical Geometries**

Vertically-Oriented Cylinder

The previous equations provide the mapping of \( \chi \) to \( B_{z,\text{ind}} \) in the most general case. Generally, the value of \( B_{z,\text{ind}} \) at a given point depends on the values of \( \chi \) at all other points, and this non-locality
complicates the extraction of $\chi$ from a measurement of $B_{z,\text{ind}}$. In the case of a thin, long, vertically-oriented prism, however, this relationship is considerably simplified.

We consider the cylindrical structure shown in Figure 1.2, with $h \gg a$. If susceptibility is zero outside the cylinder, the susceptibility map $\chi(\vec{r})$ is:

$$\chi(\vec{r}) = \chi_l \cdot \text{circ}\left(\frac{x}{a}, \frac{y}{a}\right) \cdot \text{rect}\left(\frac{z}{h}\right)$$

The Fourier transform of this expression is:

$$\tilde{\chi}(\vec{k}) = \chi_l a^2 h \cdot \text{jinc}(ak_x, ak_y) \cdot \text{sinc}(hk_z)$$

We are interested in the magnetic field pattern that results, from this:

$$B(\vec{k}) = \overline{D}(\vec{k}) \cdot \chi_l a^2 h \cdot \text{jinc}(ak_x, ak_y) \cdot \text{sinc}(hk_z)$$

Taking the inverse Fourier transform of this expression, we obtain:

$$B(\vec{r}) = \chi_l a^2 h \int dk_x dk_y e^{-jk_x x - jk_y y} \left[ \int_{-\infty}^{\infty} dk_z e^{-j k_z z} \overline{D}(\vec{k}) \cdot \text{jinc}(ak_x, ak_y) \cdot \text{sinc}(hk_z) \right]$$

First, we will evaluate the Fourier Transform integral by first integrating along $k_z$. This integral is simplified by taking advantage of the fact that sinc behaves as a nascent delta function – that is, it behaves like a Dirac delta function inside an integral when $h$ is large (which we have assumed):

$$\lim_{h \to \infty} \left[ \int_{-\infty}^{\infty} dxh \cdot \text{sinc}(hx)f(x) \right] = f(0)$$

Since $h$ is large in our integral, we can approximate it by using this property of the sinc function:

$$B(\vec{r}) \approx \chi_l a^2 \int dk_x dk_y e^{-jk_x x - jk_y y} \text{jinc}(ak_x, ak_y) \cdot \left[ \overline{D}(k_z = 0) \right]$$

$$= \frac{B_0}{3} \chi_l \text{circ}\left(\frac{x}{a}, \frac{y}{a}\right)$$

$$= \frac{B_0}{3} \chi(\vec{r})$$

Figure 1.2: A long, thin, vertically-oriented susceptibility cylinder.
The last equality holds as long as $0 < z < h$. This result is noteworthy for a few reasons. First, it means that for cases with this geometry, the relationship between field perturbation and magnetic susceptibility is local. From a measurement of magnetic field, we can calculate the susceptibility at that precise point. Second, the only important aspect of this geometry was that the z-dimension (h) was large relative to the x- and y-dimensions (a) – the particular geometry of the cross-section did not matter.

*Arbitrarily-Oriented Cylinder*

This result can be generalized to long, narrow cylinders tilted at arbitrary angles $\theta$ to $B_0$. In these cases, magnetic field variations within vessels are still local, and are multiplied by a $\theta$-dependent term [EMHaacke1997]:

$$B(\vec{r}) = B_0 \cdot \chi(\vec{r}) \cdot \frac{(3 \cos^2 \theta - 1)}{6}$$

The $(3 \cos^2 \theta - 1)$ term also appears in the spatial domain dipole kernel $d(\vec{r})$. Since, for a thin cylinder, the position vector $\vec{r}$ between any two points must be oriented at an angle $\theta$ to $B_0$, it makes sense for the field within the cylinder to depend on $\theta$ in this manner.
The MR Signal and Magnetic Field Variations

The Complex-Valued NMR Signal

The physical signal measured in MRI comes from Hydrogen nuclei (protons) located in water molecules within the human body. Prior to an MR acquisition, the subject is placed inside of a large magnetic field $B_0$ (typically 0.2-7 Tesla). This causes a small net alignment of the water protons’ magnetic moments with $B_0$, creating a macroscopic magnetization vector. When an appropriate radio-frequency (RF) pulse is applied, this magnetization vector is “tipped” to be oriented at an angle to $B_0$. Since this magnetization vector now has a component perpendicular to $B_0$, it will undergo Larmor precession and spin about $B_0$ [DNishimura2010]. The angular frequency of precession is proportional to the magnetic field B with proportionality constant $\gamma$, the gyromagnetic ratio:

$$\omega_{\text{Larmor}} = \gamma \cdot B$$

For water protons, $\gamma$ is equal to $2\pi \cdot 42.576 \, \text{MHz/Tesla}$. This phenomenon of RF energy absorption at a particular frequency is called Nuclear Magnetic Resonance (NMR).

This spinning magnetization vector induces an electrical signal in receiver coils positioned around the subject via Faraday induction. As the magnitude of the magnetization vector changes, so too does the received signal also change. However, because of Larmor precession, this signal is always modulated by the “carrier frequency” $\omega_{\text{Larmor}}$. In order to extract the actual signal of interest, this signal must be demodulated. MRI is calibrated to the Larmor frequency of water at $B_0$, the magnet field strength, so the demodulation frequency used is:

$$\omega_{\text{demod}} = \omega_{\text{Larmor},B_0} = \gamma \cdot B_0$$

However, if a particular spin at a given position experiences a slightly different magnetic field from $B_0$, this demodulation frequency will not match the actual resonance frequency of the spin. Then, demodulation will result in a time-varying phase in the demodulation signal. For a magnetic field $B_0 + \Delta B(\vec{r})$, this off-resonance frequency is:

$$\Delta \omega(\vec{r}) = \gamma \cdot \Delta B(\vec{r})$$

The time after the RF excitation pulse at which the MR signal is acquired is called the Echo Time (TE). For an acquisition at TE with a certain field offset, the final signal will have a non-zero phase given by the following equation:

$$\Delta \varphi(\vec{r}) = \gamma \cdot \Delta B(\vec{r}) \cdot TE \tag{6}$$

Thus, the MR signal is in general complex-valued, with the magnitude given by proton density, field fluctuations, and relaxation rates [DNishimura2010], and the phase given by field offsets via equation (6). Previously, it was described how magnetic susceptibility variations lead to magnetic field variations. Here, we have shown how these variations affect the phase of the NMR signal.
Effects of the MRI Acquisition on the Physical MR Signal

Image Discretization

Equation (6) holds in physical space where $\tilde{r}$ is continuous. An MR image is not continuous, but rather discrete in space.

During an MRI acquisition, it is not the image, but rather its Fourier transform that is sampled. Thinking of this as a step-by-step process, we start with a physical brain (Figure 1.3A). We then take the Fourier transform of the magnetization map $M(\tilde{r})$ associated with this image (Figure 1.3B). Physically, (1.3B) is infinite in extent and continuous. One part of the acquisition is to limit the range of points sampled (Figure 1.3C). If we zoom in on the boxed region in (1.3C) and low-pass filter it to eliminate aliasing [DNishimura2010], we see the zoomed region in (Figure 1.3D). Sampling this region on a discrete Cartesian grid, we get the discrete k-space shown in (Figure 1.3E). To obtain a discrete, finite image from the sampled data, we simply take the inverse Discrete Fourier Transform of (1.3E) to get (Figure 1.3F).

It is clear that most of the signal processing for an MRI acquisition (sampling, filtering, apodization) occurs in the Fourier domain rather than the image domain. This means that our ultimate discrete image (Figure 1.3F) is not simply a sampled version of the continuous, physical image (Figure 1.3A). However, it is elucidating to consider what the steps between (1.3A) and (1.3F) look like in the image domain. In particular, it is of interest what determines the finite resolution in the final image.

The apodization/k-space windowing illustrated in Figure 1.3C can be represented as a multiplication of the k-space intensity with a finite box:

$$\tilde{M}(k_x, k_y) \cdot \text{Rect}_{2D} \left( \frac{k_x}{W_x}, \frac{k_y}{W_y} \right)$$
In image space, this operation is equivalent to a convolution between the magnetization and the Fourier transform of the 2D Rect function, which is a 2D sinc kernel. In performing the inverse Discrete Fourier Transform, we implicitly sample this convolution, thereby obtaining a discrete image:

\[ M(x, y) * \text{sinc}_{2D}(W_x x, W_y y) \cdot \Pi_{W_x, W_y}(x, y) \]

The range of points sampled in k-space \((W_x, W_y)\) determines the resolution of our image, since it sets the size of the blur kernel (via the sinc convolution) and the spacing of the pixels (via the shah multiplication). A wider range (bigger \(W_x, W_y\)) leads to a smaller blur kernel, closer pixel spacing, and thus higher resolution - and vice-versa.

The convolution and sampling means each point in the discrete image is a weighted average of the underlying continuous magnetization map, with the weighting specified by the sinc function. One consequence of this is that the value at a particular voxel in the discrete image is determined by the values of the physical magnetization everywhere in space – not just in the volume corresponding to that voxel. This becomes easier to see when we compare a sinc averaging kernel to a rect averaging kernel (Figure 1.4) in one dimension. The rect kernel (green) has a uniform weighting at all points within the voxel, and a zero weighting for points outside it. Thus, a rect kernel average gives, for each voxel, the spatial average over all points within that voxel. For a sinc kernel (red), most of the signal at a particular voxel arises from points within it – i.e. most of the sinc signal is located between -0.5 and +0.5 voxel lengths from the sampling point. However, each the value at each voxel contains contributions from distant points in space, making that value a less-ideal measurement of the voxel’s spatially-averaged signal. Though the sinc picture is physically the correct one, I will also use the rect window at times to illustrate an “ideal” case.

**Partial-Volume Effects**

Each voxel’s complex-valued signal can be approximated as a weighted average of the complex-valued at each point inside it. When this signal is uniform across the voxel, the discrete voxel signal will be the same as the signal at each point – in a sense, the voxel signal will contain enough information to reconstruct the underlying physical signal. When signal varies across the voxel, however, a single complex-valued measurement will clearly be insufficient to infer every sub-voxel variation. This follows directly from the limited k-space acquisition.
As an illustration of how partial-volume effects can change the measured voxel magnitude and phase signals, consider the following case. A voxel overlays two tissue regions, and the signals in the two regions are spatially uniform with different magnitudes and phases. This is visualized in Figure 1.5A, where the voxel comprises two regions, Ra and Rb. Region Ra occupies a fraction $\alpha$ of the voxel, while Rb occupies the remainder, a fraction $(1 - \alpha)$.

Separately, an entire voxel of each tissue type would contribute a net signal $(M_a, \varphi_a)$ or $(M_b, \varphi_b)$ (Figure 1.5B and 1.5C).

When regions of each tissue type are combined in one voxel, we can use the “voxelization” behavior in the previous section to estimate the net voxel signal. Thus, we assume the voxel signal is a uniform spatial average over the voxel’s contents. The regions Ra and Rb will contribute their whole-voxel signals (Figure 1.5B and 1.5C) scaled by their respective voxel fractions (Figure 1.5A). These two contributions will be added to produce the final net voxel signal (Figure 1.5D).

Visually it is clear from Figure 1.5D that the difference of phase between the two regions’ signals leads to a reduced magnitude $(M_{vox})$ of the voxel signal. Quantitatively, the expressions for $M_{vox}$ and $\varphi_{vox}$ are:

\[
M = \alpha \cdot M_a
\]

\[
M = (1 - \alpha) \cdot M_b
\]
A Note on the Partial-Volume Ratio “α”

The parameter $\alpha$ in this model was introduced as the physical fraction of the voxel volume that contains a certain tissue type. However, this definition is unnecessarily restrictive. In the previous derivation of $M_{vox}$ and $\varphi_{vox}$, we only used $\alpha$ as a description of relative signal contribution of a region of tissue. This does not need to be the same thing as the physical fraction of the voxel that consists of that tissue, though using that description provides a simple, intuitive way to introduce the concept.

The relative signal contribution and physical fraction are the same when we use the “rect window spatial average” picture described previously. They are clearly not identical in the “sinc picture.” However, for a scenario with two tissue regions, to what extent does this matter? Can we still model the partial-volume behavior by a single parameter, $\alpha$?

For a one-dimensional case, suppose all of space contains either Ra or Rb (Figure 1.6). Now that we are using a sinc window for spatial averaging, the relative contribution to voxel signal from each point will be the signal at that point multiplied by the value of the sinc window at that point. To find the total contribution from an entire region (say, the blue Ra region in Figure 1.6), we need only to integrate the sinc window over the spatial extent of that region. Since we assumed that the signal is uniform across such a region, the overall contribution will be that integral.
multiplied by that signal.

We will do this for the regions of both Ra and Rb to get a “signal contribution fraction” for each. However, since sinc is normalized, its integral over all space is unity! Since the sum of these “signal contribution fractions” is equal to precisely this integral, these fractions must sum to 1 as well. Mathematically, this reduces to the same case as before: one parameter describes the signal contributions from Ra and Rb. The difference is that, in this case, \( \alpha \) does not also describe the fraction of the physical voxel volume that contains a certain tissue type, but only the degree to which each region affects that voxel’s signal.

Partial-Volume Effects and Susceptibility Measurements

The relationship between magnetic susceptibility and signal phase in Equation (6) is perfectly linear. However, (6) is only true for the physical phase and susceptibility at the sub-voxel level. If we use the measured voxel phase from a voxel that experiences partial-volume effects, then the derived susceptibility will not be meaningful. A visualization of this scenario is shown in Figure 1.7. When voxel size is larger than vessel diameter or caliber, single voxels will contain regions of both vein and parenchyma. When this occurs, voxel phase measurements are reduced relative to the actual signal phase within the vessel.

Quantitatively, recall the expressions for \( \varphi_{\text{vox}} \) and \( M_{\text{vox}} \) as a function of our model parameters:

\[
M_{\text{vox}} = \sqrt{\alpha^2 M_a^2 + (1 - \alpha)^2 M_b^2 + 2\alpha(1 - \alpha)M_a M_b \cos(\varphi_a - \varphi_b)}
\]
\[ \varphi_{\text{vox}} = \varphi_b + \tan^{-1} \left[ \frac{\sin(\varphi_a - \varphi_b) M_a \alpha}{\cos(\varphi_a - \varphi_b) M_a \alpha + M_b (1 - \alpha)} \right] \]

We are interested in voxels that contain deoxygenated (venous) blood. In these situations, we expect the susceptibility shift within veins to be given by the relationship in equation (2):

\[ \chi_{\text{vein}} = \chi_{\text{do}} \cdot Hct \cdot (1 - SvO_2) \]

For values of \( Hct = 0.4 \) and \( SvO_2 = 0.65 \), we expect \( \chi_{\text{vein}} \) to be around +0.038ppm. This is an order of magnitude larger than either gray matter (GM) or cerebrospinal fluid (CSF) susceptibility [ASchäfer2009, XHe2009, JDuyn2007]. Reported susceptibility values for GM, WM, and CSF are given in Table 1.1. These values’ predicted frequency shifts match those determined by experiment [JDuyn2007]. For voxels which are a partial-volumed mixture of vein and either GM or CSF, we can approximate the susceptibility in the GM or CSF region as zero. This is in line with studies that ignore the oxyhemoglobin-water susceptibility shift in Equation (2), as it too is an order of magnitude smaller than the deoxyhemoglobin susceptibility [APFan2014].

<table>
<thead>
<tr>
<th>Tissue</th>
<th>( \Delta \chi_{\text{water}} ) (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gray Matter</td>
<td>3.5 \times 10^{-3}</td>
</tr>
<tr>
<td>White Matter</td>
<td>5.8 \times 10^{-3}</td>
</tr>
<tr>
<td>CSF</td>
<td>3.3 \times 10^{-4}</td>
</tr>
<tr>
<td>Blood (Hct=0.4, SvO2=0.65)</td>
<td>3.8 \times 10^{-2}</td>
</tr>
</tbody>
</table>

In this situation, the phase accrued by the GM/CSF signal is zero. Going back to Equations (7) and (8), this means \( \varphi_b = 0 \) if region b (Rb) is the GM/CSF region. Now we have the following:

\[ M_{\text{vox}} = \sqrt{\alpha^2 M_a^2 + (1 - \alpha)^2 M_b^2 + 2\alpha (1 - \alpha) M_a M_b \cos(\varphi_a)} \]

\[ \varphi_{\text{vox}} = \tan^{-1} \left[ \frac{\sin(\varphi_a) M_a \alpha}{\cos(\varphi_a) M_a \alpha + M_b (1 - \alpha)} \right] \]

When \( \alpha = 1 \), then the voxel is entirely tissue type a, and \( M_{\text{vox}} = M_a, \varphi_{\text{vox}} = \varphi_a \), as expected. More generally, we now have a model for voxel magnitude and phase with 4 independent parameters \( (M_a, M_b, \varphi_a, \alpha) \) and 2 measurements \( (M_{\text{vox}}, \varphi_{\text{vox}}) \).

**Measurement of Tissue Magnitude Parameters**

Ra and Rb are tissue types, and the model parameters \( M_a \) and \( M_b \) are the expected magnitude intensities for entire voxels of those tissue types (ie with no partial-volume effects). Since we are dealing with a spoiled GRE MR acquisition, these are the \( T_2^* \)-weighted proton density image intensities. The magnitude intensities at an echo time (TE) depend on the initial magnetization \( (M_0) \) and this rate of decay \( (T_2^*) \) in the following manner:

\[ M_t(TE) = M_{t,0} \cdot e^{(-TE/T_2^*)} \]
**$M_0$ Values:** The initial magnitude intensity, $M_0$, for a given tissue class depends largely on the proton density or water fraction of that tissue. Reported values of $M_0$/water fraction for different tissues are listed in Table 1.2. Based on Gray Matter (GM) $M_0$ reported in [RBBuxton2002p164] and blood water fraction reported in [JZhao2007], we can assume that both tissue types have approximately the same $M_0$ ($\sim 1\%$ difference). The water fraction of GM reported in [XHe2009] of 84% closely matches reported GM $M_0$ values (85% in [RBBuxton2002p164]). Since CSF is approximately 100% water [XHe2009], we will use 100% for its $M_0$ value.

**$T_1$-Dependence:** In this study, GRE data was acquired with 3D excitation and two phase encode directions. The repetition time (TR) was either 26ms of 30ms and flip angle (FA) was $15^\circ$. The combination of short TR and 3D excitation leads to significant $T_1$ weighting in the final magnitude image [JZhao2007]. In effect, long $T_1$ relative to TR modulates the effective $M_0$, multiplying it by a factor $f_{T_1}$:

$$f_{T_1} = \frac{1 - e^{-\frac{TR}{T_1}}}{1 - \cos(FA) e^{-\frac{TR}{T_1}}}$$

Published values of $T_1$ and corresponding factors $f_{T_1}$ are shown in Table 1.2.

**$T_2^*$ Values:** Values of $T_2^*$ for different tissue classes have been reported in the literature. A summary is given in Table 1.2. Also shown are values estimate from 2-Echo GRE data obtained from SWI imaging. These values were estimated by fitting the observed magnitude intensities in clear tissue regions to an exponential curve. The agreement between these observed values suggests that such literature measurements are applicable to this model.

There is a dearth of reported CSF $T_2^*$ values in the literature. From one study [PPéran2007] a $T_2^*$ value of greater than 100ms was inferred for CSF. Based on our GRE data, 1000ms was measured. It is unclear what a suitable choice of $T_2^*$ for CSF is, but it is clear that the $T_2^*$ value is much longer than the observed echo times (max. TE=20ms). Thus, we will ignore $T_2^*$ decay of CSF in this model.

**$M(TE)$ Values:** For this model, we are interested in the expected magnitude intensities of pure voxels of tissue measured at our choices of echo time (TE). These values are given in the last two columns of Table 1.2. We can verify the validity of these calculations from our GRE data. First, we note that at the first echo (8.1ms) we expect GM to be more intense than CSF, while we expect roughly the same intensity at the second echo (20.3ms). This is borne out in the observations (Figure 1.8). In both the predicted case (Table 1.2) and in the observed data, CSF intensity was 0.85 that of GM at TE=8.1ms. At TE=20.3ms, the ratio of CSF intensity to GM intensity was predicted to be 1.02, while it was measured to be 1.03 in pial tissue. This is excellent agreement, and demonstrates the soundness of the GM and CSF magnitude parameters needed in the partial-voluming model. Additionally, since at TE=20.3ms, the magnitudes for
the two tissues are approximately equal, we do not need to worry which of the two tissue types is mixed in a voxel with a vein. Both have the same magnitude intensity and, as described before, both will have approximately zero phase, so they will behave identically in this partial-volume model.

It is difficult to validate the expected intensity values for blood for a few reasons. The first is that, unlike GM, venous blood does not come in many large, contiguous regions with no partial-volume effects (this analysis is meant to address precisely this issue). Thus, it is hard to find several reliable data points from which to derive a precise measurement. That said, there are some large regions of blood in the brain – notably the superior sagittal sinus. However, the magnitude intensity of the superior sagittal sinus is unreliable. Its proximity to receive coils gives it artificial hyperintensity. Additionally, suspected inflow effects mean that its magnetization does not have time to reach the steady-state equilibrium of the TR=26ms excitations. This effectively means that, like arteries, the factor $f_{T_1}$ in Table 1.2 is an overestimate of the signal attenuation factor (ie the actual $T_1$ attenuation factor is, in reality, closer to 1). As such, the closest we could get to validating this model in the case of blood was to check the transverse relaxation time $T_2^*$, as it does not depend on the initial magnetization. The measured blood values are given in Table 1.2, and are in close agreement with the model.

The predicted ratio of blood signal magnitude to GM signal magnitude from this analysis is approximately 0.75. This is the number that was used in subsequent analysis.

*Estimating Parameters from Net Voxel Signal*

In MR, we acquire magnitude and phase measurements at each point. This is equivalent to having measurements of $M_{\text{vox}}$ and $\varphi_{\text{vox}}$ in EQS MAGPHIVOX. Since we reliably know $M_a$ and $M_b$ as described above, we are left with only two unknown parameters, $\varphi_a$ and $\alpha$. We can solve for these two unknowns as a function of the measurements ($M_{\text{vox}}$ and $\varphi_{\text{vox}}$) and the known parameters ($M_a$ and $M_b$). This expression has a closed-form analytic solution. The solution for $\hat{\alpha}$ is given by a root of a quadratic

<table>
<thead>
<tr>
<th>Tissue</th>
<th>$M_0$ (normalized to water)</th>
<th>$T_2^*$ (Literature)</th>
<th>$T_2^*$ (measured from data [6])</th>
<th>$T_1$</th>
<th>$f_{T_1}$</th>
<th>$M_t(8.1,\text{ms})$</th>
<th>$M_t(20.3,\text{ms})$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gray Matter</td>
<td>0.85 [1]</td>
<td>59.6ms [3]</td>
<td>50ms (occipital)</td>
<td>1820ms [7]</td>
<td>0.297</td>
<td>0.220</td>
<td>0.180</td>
</tr>
<tr>
<td></td>
<td></td>
<td>66.0ms [4]</td>
<td>67ms (pial)</td>
<td></td>
<td></td>
<td>0.223</td>
<td>0.185</td>
</tr>
<tr>
<td>White Matter</td>
<td>0.80 [1]</td>
<td>53.2ms [4]</td>
<td>[I SHOULD DO THIS]</td>
<td>1084ms [7]</td>
<td>0.416</td>
<td>0.286</td>
<td>0.227</td>
</tr>
<tr>
<td>CSF</td>
<td>1.00 [1]</td>
<td>&gt;100ms [5]</td>
<td>=1000ms</td>
<td>3300ms [8]</td>
<td>0.188</td>
<td>~0.188</td>
<td>~0.188</td>
</tr>
<tr>
<td>Blood (Venous)</td>
<td>0.86 [2]</td>
<td>25.0ms [2]</td>
<td>25.0ms (occipital)</td>
<td>1584ms [9]</td>
<td>0.327</td>
<td>0.203</td>
<td>0.125</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29.2ms (pial)</td>
<td></td>
<td></td>
<td></td>
<td>0.213</td>
<td>0.140</td>
</tr>
</tbody>
</table>

Table 1.2: $T_2^*$ and $M_0$ values for tissue types, and the expected signals at different echo times. Both published values and values measured from our data are shown. [1](RBBuxton2007p164); [2](JZhao2007); [3](SPunwani1997); [4](APeters2007); [5](PPéran2007); [6](APFan2014); [7](GJStanisz2005); [8](NGelman2001); [9](HLu2004).
equation:
\[ \hat{\alpha}^2 \cdot [M^2_a - M^2_B] + \hat{\alpha} \cdot [2M^2_B - 2M_{\text{VOX}}M_b \cos(\varphi_{\text{VOX}})] + [-M^2_{\text{VOX}} - M^2_B + 2M_{\text{VOX}}M_b \cos(\varphi_{\text{VOX}})] = 0 \]

From this solution for $\hat{\alpha}$, we can find $\hat{\phi}_a$:

\[ \hat{\phi}_a = \sin^{-1}\left(\frac{M_{\text{VOX}} \sin(\varphi_{\text{VOX}})}{\hat{\alpha} \cdot M_a}\right) \]

From $\hat{\phi}_a$ and Equation (6) we can estimate the susceptibility in Region A, i.e., the vein susceptibility:

\[ \hat{\chi} = \frac{6}{(3 \cos^2(\theta) - 1) \cdot \gamma \cdot B_0 \cdot TE} \]

**Factors Ignored in this Model**

**Field Variations Outside Tilted Vessels**

For nearly-vertical vessels tilted a small angle away from $B_0$, there will be magnetic field variations outside the vessels themselves. This is given by [RMWeisskoff1992]. This violates the assumption that in our two-region model, the complex signal in each region is uniform. Intravoxel phase variations of this kind will lead to additional $T_2^*$ magnitude decay. This is explored in the Discussion section.

**Effects of SvO$_2$ on Blood $T_2$ and $T_2^*$**

It is well-documented that the transverse relaxation rate $T_2$ of blood depends on the blood’s oxygenation state, and that this change effects a change in the $T_2^*$ decay of blood signal [HLu2012, MJSilvennoinen2003]. For simplicity, and to arrive at an analytic solution, this method assumes a fixed $T_2^*$ with no SvO2 dependence.

**Determining Vessel Orientation Relative to $B_0$**

One final parameter is needed in this model – the tilt angle $\theta$. It is needed to extract the susceptibility from the measured phase:

\[ \hat{\chi} = \hat{\phi}_a \cdot \frac{6}{(3 \cos^2(\theta) - 1) \cdot \gamma \cdot B_0 \cdot TE} \]

In this analysis, a direct measurement of $\theta$ was performed from the data. The first step in this analysis was to create an ROI mask that identified voxels belonging to a given blood vessel. By performing a 3D linear regression on the coordinates of these mask voxels, we get an analytical estimate for the orientation of the vessel. From this expression, we can directly measure $\theta$.

The $R^2$ value for this regression also tells us how good the approximation of a long, thin cylinder is for a given vessel.
Part 3: Methods

Summary

Several steps are required to go from magnitude and phase images to JUMP estimates of OEF. These steps are described in this section.

Preprocessing of Magnitude and Phase Images

Magnitude Image

The GRE magnitude image requires minimal preprocessing for it to be used for JUMP analysis. As shown in Figure 1.9, the image contains the proper contrast for quantitative JUMP, and is free of confounding artifacts.

The only artifacts of note in the magnitude are inflow effects and coil sensitivity effects. This sequence is 3D-encoded with a short TR (30ms), so there is a steady-state initial magnetization for each tissue that is significantly lower than its fully-relaxed value. However, when blood from outside the excitation slab enters the imaging area, it does not initially have the appropriate steady-state magnetization. Rather, it has an initial value closer to its much larger fully-relaxed value. As a result, such blood appears hyperintense in these GRE magnitude images. This is apparent from Figure 1.9A – the yellow arrow points to such hyperintense blood in cerebral arteries. When applying JUMP, it is important to ensure that the blood vessel being analyzed does not suffer from such inflow effects, as the different magnitude intensity conflicts with the assumptions in the JUMP model.

The other notable artifact is a presumed coil sensitivity-related intensity near the front and rear of the brain. This is shown circled in blue in Figure 1.9A, on the right of the image. This artifact is not significant.
in JUMP, as it only affects large-scale variations in intensity – the crucial small-scale intensity variations
due to blood vessel/parenchyma dephasing are not altered.

*Brain Mask Creation*

Many steps for processing the phase image require a binary mask that identifies the “brain.” However, it
is difficult to generate such a mask reliably from the phase image. The magnitude image, since it does
not require any special preprocessing, is ideal for creating this mask. I created these masks by using the
FSL Brain Extraction Tool (BET) [MJenkinson2005]. This is an automatic tool that segments a brain
region-of-interest (ROI) from an image of a head. This tool requires several fine-tuned parameters to
achieve an optimal segmentation, but is otherwise a simple and reliable tool for creating brain masks.

*Phase Image*

The phase image requires significant preprocessing before it can be used in JUMP analysis. This is
primarily due to large-scale susceptibility artifacts and phase wrapping.

*Figure 1.10:* (A) Raw reconstructed phase image. Note the phase wrapping within the brain, and the speckled pattern outside it. This is due to the low SNR outside the brain – zero-magnitude-mean complex noise has a uniform phase distribution between negative pi and pi. (B) Masked phase image. (C) Unwrapped, masked phase image (D) Phase image where harmonic background phase variations have been removed with SHARP
Figure 1.10 illustrates a raw phase image (A) and the effects of masking (B), phase unwrapping (C), and harmonic artifact removal (D). Each step is crucial in preparing the phase image for JUMP, MR susceptometry, and QSM analysis.

**Masking**

Masking is done by simply multiplying the phase image by the binary brain mask obtained from the magnitude image. The result is shown in Figure 1.10B.

**Phase Unwrapping**

After this, we turn our attention to the phase wraps in the brain. From Equation (6), we know that signal phase is proportional to the local magnetic field offset. However, because phase can only physically take on values between $-\pi$ and $\pi$, these “real” phase values are always “wrapped” to within that range. An important step is to “unwrap” the phase image so that physically meaningful information about magnetic field variations is restored.

Phase unwrapping was done with the Robustunwrap algorithm using free MATLAB code developed by Cusack et al. [RCusack2002]. This method uses a path-based unwrapping approach, where the number of phase discontinuities in a path between two points is presumed to equal the number of phase “wraps” between those two points. The main benefit of this implementation, however, is that it uses the corresponding magnitude image to weight the different “unwrapping paths.” By using a magnitude image that is multiplied with the brain ROI mask, we can ensure that all “unwrapping paths” that travel outside the brain are ignored by the algorithm. This is important, since by masking the brain, we have removed any physically meaningful information outside of it.

Previous work has used Laplacian phase unwrapping for this step. This works by taking the Laplacian of the phase image, followed by the inverse Laplacian. The image Laplacian is calculated in such a way that it is insensitive to phase wraps, so when the inverse Laplacian is taken, the result is an unwrapped version of the initial image [MASchofield2003]. However, calculating the inverse Laplacian requires imposing known boundary conditions at the edges of the region to be unwrapped. In our case, we only wish to unwrap the Laplacian over the brain mask ROI, and imposing the appropriate boundary conditions on this region’s arbitrary-shaped boundary is non-trivial. As such Laplacian unwrapping introduces artifacts and phase variations into the unwrapped image, and is unsuitable for this application.

**Harmonic Artifact Removal**

Figure 1.10C shows a masked, unwrapped phase image. At this point, the tissue contrast is still dominated by a large, smooth spatial variation in signal phase. This field variation is due to the large susceptibility mismatches between the brain, skull, sinus, and external air. There are two main approaches for eliminating this background phase pattern: high-pass filtering and harmonic signal removal.
High-pass filtering exploits the fact that this background field pattern consists primarily of low spatial frequencies, while susceptibility structures of interest (blood vessels, punctuate iron sources) consist primarily of high spatial frequencies. Thus, by high-pass filtering the phase image, we can in principle remove the undesired phase variations and preserve the desired ones.

The issue with high-pass filtering is that even the background field pattern contains high-spatial-frequency components near the edges of the brain. Thus, even after high-pass fileting to remove phase variations, significant artifacts remain, especially near the brain edges (Figure 1.11A). Since many blood vessels of interest are near the edge of the brain, this is a major drawback of Fourier-domain high-pass-filtering.

To obtain superior background phase removal, we first note that the background phase variations originate outside the brain ROI. This fact means that, over the brain ROI, the background phase variations are harmonic – ie, the Laplacian of them is zero. Several techniques exploit this fact for improved background phase removal. In my work, I used a method called Sophisticated Harmonic Artifact Removal for Phase data (SHARP) [FSchweser2011]. SHARP exploits the spherical mean value property of 3D harmonic functions, which says that a spherical averaging kernel applied to any region of a harmonic field will equal the value at the center of the sphere. An illustration of a SHARP-processed phase map is shown in Figure SHARPHPF (B). The improvement over the high-pass-filter-processed phase image is pronounced, especially near the image edges.

**Vessel ROI Identification and Masking**

I wanted to obtain blood vessel OEF estimates using JUMP, and to compare those estimates to those obtained using conventional methods. This required identification of a vessel ROI to select voxels from which to obtain quantitative OEF estimates. I manually identified voxels corresponding to particular blood vessels of interest and saved this information as a binary mask for each vessel. Because JUMP is limited in applicability to nearly-vertical blood vessels, my masking and further analysis was limited to such vessels. These masks identified anatomical structures, and were also used to automatically make

*Figure 1.11: (A) Phase image processed with Fourier high-pass-filter to remove background field variations (B) Same section, with background phase variations removed with SHARP (C) Unprocessed, raw phase image*
measurements via MR susceptometry, and from QSM-reconstructed susceptibility maps.

Once specific voxels were identified, it was possible to perform MR susceptometry and JUMP OEF estimation. By looking at the phase image and magnitude image values at those voxel locations, it was possible to estimate OEF using the equations described in the Theory section.

**Creation of QSM-Reconstructed Susceptibility Maps**

QSM describes a family of techniques for creating spatial susceptibility maps of the entire brain from GRE phase data by inverting the dipole kernel mapping from susceptibility to phase, as described in Theory. In order to compare JUMP oxygen saturation measurements to the oxygen saturation estimates obtained from a QSM-reconstructed susceptibility measurement, I needed to perform the QSM dipole inversion. This was performed using a freely available QSM toolbox [BBilgic2014]. To generate the QSM maps used in this analysis, I used a magnitude-weighted L1-regularization penalty on the gradient of the phase image.
Part 4: Results

Numerical Simulation Results

Illustration of How the Method Works

The use of a two-compartment model to estimate susceptibility and partial-voluming can be summarized as extracting two unknown parameters \((\varphi_a, \alpha)\) from two measurements (mag, phase). The fact that this works can be visualized plotting signal magnitude and phase at different points in \((\varphi_a, \alpha)\)-space. To do this, we use Equations (7) and (8) to calculate what signal magnitude would be for each \((\varphi_a, \alpha)\) point. We then display the results as an image. The x- and y- axes correspond to \(\alpha\) and \(\varphi_a\), and image color corresponds to the value of the signal magnitude (Figure 1.12). Likewise, we can show the same image for phase, instead of magnitude.

These images provide an intuitive explanation of why this method works. Suppose we have a measurement of magnitude and phase from a particular voxel. If we highlight all points in the \((\varphi_a, \alpha)\)-plane that result in the desired magnitude, we get the curve shown in (Figure 1.12A). This curve defines a set of valid \((\varphi_a, \alpha)\) points. If we do the same thing with phase, we get a second curve in \((\varphi_a, \alpha)\)-space, shown in (Figure 1.12B). As can be see, these curves will, in general, intersect at a single point. This point is that estimated \((\hat{\varphi}_a, \hat{\alpha})\) that we calculate from Equations (7) and (8). Intuitively, we can see why this works.

Magnitude: From the \((\varphi_a, \alpha)\) versus magnitude image (Figure 1.12A), we can see that signal magnitude decreases as we move towards a given point in the middle of the \((\varphi_a, \alpha)\)-plane. This occurs when both voxel regions have signals of identical magnitude, and when vessel phase equals \(\pi\). At this point, there is perfect dephasing within the voxel, and the resulting signal magnitude is zero. Any change in either \(\alpha\) or \(\varphi_a\) about this point leads to less dephasing, and thus higher signal magnitude. This can be seen (Figure 1.12A) by the “rings” of constant magnitude in \((\varphi_a, \alpha)\)-space.

Phase: Conversely, measured phase tends to increase with larger \(\alpha\) and larger \(\varphi_a\), as long as \(\varphi_a\) is less than \(\pi\). This can be argued from the signal model: all of the phase in the measured signal comes from the “vein” signal phase, \(\varphi_a\). With increasing \(\alpha\), a greater fraction of the measured signal comes from the vein, and with increasing \(\varphi_a\), that portion of signal has a greater phase. Thus, it is logical that an increase in either would lead to an increase in measured voxel phase.

One \(\varphi_a\) goes above \(\pi\), the situation is flipped. Previously, we argued that brain tissue has \(\varphi_b = 0\). However, in this case, it is helpful to consider its phase as \(\varphi_b = 2\pi\). Now, the opposite is true: a lower \(\alpha\) actually gives a higher measured phase at a given value of \(\varphi_a\). Previously, dephasing tended to decrease the measured phase by bringing it closer to zero. In this case, dephasing tends to increase the measured phase by bringing it closer to \(2\pi\).

This behavior is also apparent in the phase image (Figure 1.12B). Now, lines of constant phase form “spokes” in \((\varphi_a, \alpha)\)-space. In fact, a given phase measurement determines a “spoke” in \((\varphi_a, \alpha)\)-space, but a magnitude measurement determines a “ring” in \((\varphi_a, \alpha)\)-space. As is shown, these two curves
generally intersect at a single point: the solution. These images show that GRE magnitude and GRE phase provide complementary information about vessel phase ($\varphi_a$) and partial-voluming ($\alpha$). Susceptibility-weighted scans acquire GRE principally for the phase image, though the magnitude is also acquired. Here, we see that this magnitude image contains precisely the sort of information we need to remove partial-volume effects in the phase image.

**Demonstration on Simulated Low-Resolution GRE Acquisitions of Susceptibility Cylinders**

**Vessel Creation Protocol**

This method was tested on simulated low-resolution acquisitions of cylindrical vessels. To do this, a 3D image of a cylindrical vessel was created (image size: 200x200x200; vessel radius: 5). Vessel OEFs were: 0.1, 0.2, 0.3 and 0.4. Tilt angles were 0, 10, 20, 30, and 40 degrees. Acquisition resolutions were: 20, 16.7, 14.3, 12.5, 11.1, 10, 8.3, 7.7, 7.1, and 6.7. Additionally, vessels were simulated at different offsets from the origin of 0, 4, 8, and 12 pixels. Images of simulated susceptibility cylinders are shown in figure Figure 1.13.

Parameters used in these simulations were: $TE = 20ms$; $B_0 = 2.89T$; Vein-to-parenchyma intensity ratio = 0.75.

To run the simulations, a full-resolution (200x200x200) vessel image was created that had the proper OEF, Tilt Angle, and vessel offset. The Fourier Transform of this image was multiplied by the Dipole Kernel to generate a field offset map $\Delta B_2(\mathbf{r})$. This map, combined with TE and B0, was in turn used to generate a phase map. The vessel/parenchyma magnitude was known a priori at each point. Combining these magnitudes and the phase map gave a complex-valued physical signal map at full resolution.
In order to simulate a low-resolution acquisition, this complex-valued image was cropped in k-space to the suitable size. Taking the inverse Fourier Transform of these k-space images gave the final simulated low-resolution vessel images (Figure FIGCHICYLSIM). The simulated low-resolution vessel acquisitions were analyzed with the same pipeline used for in vivo data, described in the Methods section.

**Numerical Vessel OEF Estimation Results**

I wished to assess the performance of JUMP on numerical vessels in two ways: (1) by measuring how accurate its OEF estimates were at different resolutions when compared to direct measurement via MR
susceptometry or QSM susceptibility map, and (2) by observing whether there was a bias in JUMP’s OEF estimates towards any particular range of OEF values.

Comparison of JUMP with MR susceptometry and QSM is shown in Figure 1.14A. Using either MR susceptometry or QSM – neither of which accounts for partial-volume effects in the phase image, we see that the estimated OEF drops off precipitously as voxel size increases. Even at small voxel sizes, we note that OEF estimates using these methods are highly variable: sometimes they are higher, and sometimes they are lower than the true vessel OEF. However, OEF estimates from JUMP are consistent across all acquisition resolutions. Never does the JUMP OEF estimate deviate more than 10% from the true vessel OEF. This suggests that indeed, JUMP properly accounts for partial-volume effects between veins and parenchyma.

However, we observe biases in JUMP’s OEF estimates if we run JUMP on several vessels with different OEF. This is shown in Figure 1.14B. Here, we have simulated low-resolution acquisitions of five different numerical vessels at all resolutions. The five vessels had the same tilt angle (20 degrees) and voxel offset (zero), and had true OEFs of 0.1, 0.2, 0.3, 0.4, and 0.5. As shown in the plot, JUMP obtained consistent measurements across a range of acquisition resolutions for all vessels. However, at low OEF (0.1), the estimates were biased upwards. That the estimated OEF was consistently higher than 0.1 for this vessel suggests that JUMP has an intrinsic bias towards higher OEF estimates. Additionally, for higher OEF, it was observed that JUMP begins to fail at a certain resolution. The failure mode was not to give incorrect OEF estimates, but to obtain complex-valued OEF estimates, which are physically incorrect and meaningless.

Figure 1.14: (A) OEF estimation from numerical vessel at different-resolution acquisitions using three different methods. JUMP obtains consistent measurements as voxel size varies, while direct MR susceptometry measurement and direct QSM measurement are highly variable. (B) JUMP OEF estimates in simulated vessels with different OEF across all acquisition resolutions. At low OEF values, estimates are biased upwards, but otherwise, OEF is accurate and consistent as voxel size varies.
Simulated Low-Resolution Acquisition of Existing in vivo Data

This method was tested on previously-acquired data [APFan2014]. Vessels that did not experience partial-volume effects were identified, and their susceptibilities measured. Then, the images were cropped in k-space as a means of simulating a lower-resolution acquisition. The same vessels were identified in the resulting low resolution images. From the quantitative values in the low-resolution images, we measured susceptibility directly from phase, by using a regularized QSM reconstruction, and by using the method proposed here. Direct measurement and QSM reconstruction yielded inaccurate susceptibility measurements due to partial-voluming of vein and parenchyma, but the method proposed here gave accurate measurements even when partial-volume effects were present.

The acquisition was a 2-echo GRE (TE=8.1ms, 20.3ms), FA=15°, TR=26ms, with phase encoding along y and z. It was acquired at 3T with GRAPPA factor R=2x1. Both magnitude and phase were separately saved for each channel, and then combined using separately-measured coil sensitivity maps. The native resolution of the acquisition was 0.6mm isotropic. This acquisition was cropped in k-space to yield images with 1.2mm, 1.8mm, and 2.4mm isotropic voxel sizes.

Effects of Apodization Window Shape

As described before, the MR acquisition only acquired a finite extent of k-space. This uniform k-space weighting across a rectangular extent of k-space is equivalent to multiplying all of k-space by a rect window function. In image space, this is equivalent performing spatial averaging with a sinc window kernel. The partial-voluming model used here assumes the side lobes of this sinc window do not contribute significantly.

In order to test the validity of this premise, low-resolution acquisitions were simulated using two different k-space window functions. In the first case, the k-space representation of the 3D image was multiplied by a Sinc window (Figures 1.15-18, tops). In the second case, the k-space representation was multiplied with a Rect window (Fiure 1.15-1.18, bottoms). The Fourier transforms of these windows are the image-domain kernels used for blurring (Figure 1.16 and 1.18). As can be seen in the kernel plots, using the Sinc window for k-space apodization gives much smaller side lobes in the image-domain averaging. This more accurately reflects the assumptions of this method, which assumes a finite-extent averaging kernel.

The images were cropped in k-space, then transformed to the image domain. Finally, the images were undersampled by the appropriate undersampling factor in each dimension to obtain low-resolution images. This was done for undersampling factors of 2x and 4x, giving images with resolutions of 1.2mm and 2.4mm isotropic, respectively. In order to test what difference apodization window shape made, a pial vessel (identified in images) was identified and, and its susceptibility measured using the method proposed here (results listed in Table 1.3). For the 1.2mm voxel size acquisition, the sinc-windowed version was 4.4% lower than the rect-windowed version. For 2.4mm, the same figure was 6.2%. These small differences are smaller than other sources of variation, suggesting that the spatial-averaging approximation inherent in this method is sound.
Figure 1.15: Low-resolution GRE image obtained by numerically cropping k-space data. Nominal 1.2mm$^3$ voxel size. (Top-Sinc) Native-resolution k-space data was multiplied by sinc window. Data was transformed back to image domain and sampled. (Bottom-Rect) Native-resolution k-space data was multiplied by rect window. The resulting cropped k-space data was transformed into the image domain to directly obtain the undersampled image. Undersampling factor=2

Figure 1.16: (A) K-space windows used to crop image for simulating a low-resolution acquisition. This is a view along kx at one value of (ky,kz). (B) Image-domain kernels corresponding to k-space windows. This is a view along x at (y=0,z=0). Undersampling factor=2

Figure 1.17: Low-resolution GRE image obtained by numerically cropping k-space data. Nominal 1.2mm$^3$ voxel size. (Top-Sinc) Native-resolution k-space data was multiplied by sinc window. Data was transformed back to image domain and sampled. (Bottom-Rect) Native-resolution k-space data was multiplied by rect window. The resulting cropped k-space data was transformed into the image domain to directly obtain the undersampled image. Undersampling factor=4

Figure 1.18: (A) K-space windows used to crop image for simulating a low-resolution acquisition. This is a view along kx at one value of (ky,kz). (B) Image-domain kernels corresponding to k-space windows. This is a view along x at (y=0,z=0). Undersampling factor=4
**Effects of Different Resolution**

One pial vein was measured at different resolutions using JUMP, MR susceptometry, and QSM. The vein and estimated OEF are shown in Figure 1.19. As shown in the plot, estimated OEF is consistent across all simulated low-resolution acquisitions with JUMP, whereas direct measurement from phase or from reconstructed susceptibility yields resolution-dependent results.

Table 1.3: Summary of JUMP OEF estimates for several veins. Veins were measured at several simulated low resolutions using two different window shapes. As shown, there was no notable difference between whether a sinc or rect window was used for k-space cropping, suggesting the uniform spatial averaging assumption is valid.

<table>
<thead>
<tr>
<th>Vein</th>
<th>OEF Measurement (w/Method)</th>
<th>Rect/Sinc Diff.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.6mm (Rect)</td>
<td>0.6mm (Sinc)</td>
</tr>
<tr>
<td>1</td>
<td>.399±.046</td>
<td>.362±.060</td>
</tr>
<tr>
<td>2</td>
<td>.329±.033</td>
<td>.302±.037</td>
</tr>
<tr>
<td>3</td>
<td>.328±.017</td>
<td>.256±.026</td>
</tr>
<tr>
<td>4</td>
<td>.410±.042</td>
<td>.312±.070</td>
</tr>
<tr>
<td>5</td>
<td>.385±.039</td>
<td>.366±.034</td>
</tr>
<tr>
<td>6 (big)</td>
<td>.371±.033</td>
<td>.334±.057</td>
</tr>
</tbody>
</table>

Figure 1.19: (Bottom) Illustration of SHARP phase image identifying vessel measured. (Top-Left) Zoomed views of vessel in simulated low-resolution acquisitions. (Bottom-Left) Plot of estimated OEF vs. simulated acquisition resolution. OEF was estimated in this vein using JUMP, direct phase measurement (MR susceptometry), and direct susceptibility measurement from QSM-reconstructed susceptibility map.
In Vivo Experiments

The previous section described the analysis of in vivo data, but relied on numerical undersampling to assess the performance of JUMP at different resolutions. Using JUMP to measure OEF in veins from MR acquisitions with different native resolution is a more realistic assessment of its performance. I acquired flow-compensated data from two volunteers, identified veins, and estimated OEF with JUMP, MR susceptometry, and QSM inversion.

For each of the two volunteers, several blood vessels were identified. Using the protocol described in the Methods section, OEF was measured from each by JUMP, MR susceptometry, and QSM.

Protocol and Acquisition Parameters

Flow-compensated, 2-echo GRE images were acquired from two male subjects at five different resolutions. Acquisition parameters are summarized in Table 1.4 [APFan2014]. Additionally, low-resolution head and body coil images with the same FOV as the GRE acquisitions were acquired throughout the scan. These were used for ESPIRiT/SENSE reconstruction, which enabled a fourfold acceleration factors without the need for unnecessarily long GRAPPA reconstruction. ESPIRiT/SENSE reconstruction was performed using the freely-available BART toolbox [MUecker2015]. No partial Fourier was used in any acquisition.

<table>
<thead>
<tr>
<th>Resolution</th>
<th>TA</th>
<th>TE₁/TE₂</th>
<th>TR</th>
<th>Flip Angle</th>
<th>Bandwidth</th>
<th>Accel. Factor (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.6x0.6x0.6mm</td>
<td>10m23s</td>
<td>8.1ms/20.3ms</td>
<td>30ms</td>
<td>15°</td>
<td>260 Hz/Px</td>
<td>2x2</td>
</tr>
<tr>
<td>0.7x0.7x0.8mm</td>
<td>7m35s</td>
<td>8.1ms/20.3ms</td>
<td>30ms</td>
<td>15°</td>
<td>260 Hz/Px</td>
<td>2x2</td>
</tr>
<tr>
<td>0.9x0.9x0.9mm</td>
<td>5m13s</td>
<td>8.1ms/20.3ms</td>
<td>30ms</td>
<td>15°</td>
<td>260 Hz/Px</td>
<td>2x2</td>
</tr>
<tr>
<td>1.2x1.2x1.5mm</td>
<td>2m21s</td>
<td>8.1ms/20.3ms</td>
<td>30ms</td>
<td>15°</td>
<td>260 Hz/Px</td>
<td>2x2</td>
</tr>
<tr>
<td>1.8x1.8x1.8mm</td>
<td>1m21s</td>
<td>8.1ms/20.3ms</td>
<td>30ms</td>
<td>15°</td>
<td>260 Hz/Px</td>
<td>2x2</td>
</tr>
</tbody>
</table>

Images and Vessels

Images from both subjects are shown in Figure 1.21. This image is a sagittal maximum-intensity-projection (MIP) over several slices of the QSM-reconstructed susceptibility map. The QSM susceptibility maps were used for visualization of anatomical structure because all vessels appear with approximately the same contrast, unlike with unprocessed phase images. Many blood vessels are visible in both MIPs. Three are identified and numbered in each subject, and these six total vessels were analyzed in more detail.
Figure 1.22 shows veins 4 and 5 from Figure 1.21 in more detail. The vessels can be discerned at all acquisition resolutions, though it becomes less intense as voxel size becomes very large. OEF measurements were made from these images using the measurement protocol.

**OEF Estimates Using All Methods**

Figure 1.20 shows estimated OEF for the six veins identified in Figure 1.21. Plot numbers correspond to vein numbers in Figure 1.21. In all cases it is observed that JUMP gives more consistent estimates across different resolutions than either MR susceptometry or QSM, and that its measurements are within reported physiological ranges.

Figure 1.20: Plots (1) through (6) correspond to the number veins in Figure BRAINSAGMIPS. For all measurements, JUMP gives a more accurate measure of OEF across different resolutions. In plots (3) and (6), only five data points are plotted for JUMP estimation.
Figure 1.21: Susceptibility map sagittal MIPs showing pial veins. Three veins are identified in each subject for quantitative OEF estimation using MR susceptibility, QSM, and JUMP.

Figure 1.22: Close-up of veins 4 and 5 from Subject 2 above. Both veins are shown in the zoomed SHARP phase images at all five acquisition resolutions at bottom.
Part 5: Discussion

**JUMP Is Robust to Partial-Volume Effects**

In numerical and in vivo experiments, JUMP provided consistent OEF measurements at different acquisition resolutions. In contrast, both QSM and MR susceptometry give variable OEF estimates at different acquisition resolution due to partial-volume effects. This point is illustrated in Figure 1.23. Here, in both numerical and in vivo results, it is shown that OEF estimates from JUMP are consistent, even as voxel size becomes larger than vessel size. This is contrasted with direct measurement from the phase image (MR susceptometry) or reconstructed susceptibility map (QSM), where OEF estimates vary with voxel size. Also, once the voxel size is larger than the vessel diameter, the estimates from MR susceptometry and QSM drop precipitously due to partial-volume effects. In terms of obtaining accurate OEF measurements for specific blood vessels, JUMP therefore has several advantages over techniques that do not account for partial-voluming.

**JUMP Absolute Accuracy**

Estimations of OEF using JUMP on simulated, numerical vessels suggested a bias towards larger OEF estimates. This is apparent from Figure 1.24, where the vessel with low OEF was estimated to have a significantly higher value when using JUMP. In particular, the vessel with OEF of 0.1 was estimated to have OEF between 0.15 (at higher resolution) to 0.2 (at lower resolution). These estimates had low associated measurement uncertainty, and this measurement error did not explain the deviation from

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**In vivo**

**Simulation**

![Figure 1.23: OEF estimates from a single blood vessel taken from in vivo data and a single vessel from numerical simulation](image)
0.1. Thus, it is believed that JUMP, as currently implemented, has a bias away from very low OEF values.

A possible explanation for this relates to the modeling of a voxel as a two-compartment volume, with coherent signal within each compartment. While this may be, in theory, correct for perfectly vertical vessels, it is not generally accurate. With vessel tilt, it is documented that magnetic field varies over small distances outside of the vessel [RMWeisskoff1992]. This extravascular field variation will lead to further dephasing and magnitude attenuation, and will also affect the measured voxel phase of the acquired image. It is thought that both effects contribute to error in estimated OEF, depending on both vessel susceptibility and tilt angle. However, since such field variations are fixed and well-characterized, it is possible to account for them when obtaining JUMP OEF estimates.

**Quantification of Uncertainty and Reduction of Measurement Error**

When using either MRI susceptometry or QSM to obtain absolute, quantitative measurements of OEF in particular blood vessels, one must manually select which voxels are suitable to be measured. This results in a difficult tradeoff – more vessels will give a measurement with less uncertainty, but ideally, only vessels that do not exhibit partial-volume effects should be used. This is difficult to do, as it requires knowing *a priori* which voxels do not suffer from partial-volume effects. Additionally, as shown in Figure 1.23-Simulation, the voxels with the highest phase and susceptibility values in a particular vessel often give overestimates of OEF. Thus, obtaining OEF measurements using MR susceptometry or QSM requires dealing with partial-volume effects and OEF underestimates, potential OEF overestimates, and small sample sizes. All these factors mean that OEF estimates from blood vessels that are obtained with these methods have several sources of error, and are not very accurate.

In contrast, JUMP – by obtaining accurate OEF estimates from voxels that suffer from partial-volume effects, enables a much larger number of voxels to be used to make measurements. Since voxels with partial-volume effects are allowed, one does not need to *a priori* select voxels without them. As shown in Figure 1.24, this results in more-accurate OEF measurements and, crucially, allows the measurement uncertainty to be quantified. With previous methods, it is not possible to reliably quantify the measurement error in this way.
Part 6: Conclusion

JUMP provides OEF estimates in blood vessels that are robust to partial-volume effects and have higher absolute accuracy than MR susceptometry or QSM OEF estimates. By obtaining useful measurements from voxels that suffer from partial-volume effects, it enables more samples to be taken from a given blood vessel, which reduces and quantifies the measurement uncertainty. However, JUMP has bias in its estimates – in particular, it is biased away from very low OEF estimates. In spite of these biases, JUMP preserves OEF differences in blood vessels and provides consistent measurements across voxel size. Both of these suggest that, even if OEF estimates from low-susceptibility vessels are not absolutely accurate, partial-volume effects are still accounted for. Thus, comparisons can be made between vessels without worrying about different levels of partial-voluming in them.
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Chapter 2

Measuring in vivo Fetal Motion with MRI Using Volumetric Navigators (vNavs)

Part 1: Introduction

The most significant aspects of cognitive development occur during the fetal period. However, existing techniques for imaging the fetus in utero do not for detection of brain pathology during this vital stage. MRI provides excellent soft tissue contrast within the brain and is routinely used to diagnose brain abnormalities in adults, and fetal diagnoses would similarly benefit from this technology [YYamashita1997]. However, the current state of fetal MRI does not enable such diagnoses to be consistently made in utero. Thus, there is a need for development of MRI technologies that enable diagnostic-quality imaging of the fetal brain.

The main hurdle in the development of fetal MRI is the motion of the fetus, which can severely compromise image quality. Existing techniques for motion correction in fetal MRI exist, but may fail when there is significant motion [FRousseau2006]. Recently, however, it was proposed to use volumetric navigators (vNavs) embedded within a longer MR sequence to prospectively correct for motion [MDTisdall2012]. However, it was unknown whether vNavs can be used to measure motion in the fetus.

In my work, demonstrate that, vNavs can be used to accurately measure fetal motion, even when that motion is severe. This is a valuable contribution to fetal MRI development, as it suggests that vNavs can be used to prospectively correct for fetal motion, thereby enabling diagnostic-quality images to be obtained in utero.
**Part 2: Theory**

**Rigid Body Motion**

A full description of the position of a rigid body in three-dimensional space requires six degrees of freedom – three to describe its translational position, and three to describe its angular orientation. Physically, we consider the fetal head to be a rigid body – as it moves, we do not expect it to deform. This is not entirely accurate – field inhomogeneity in MR induced by susceptibility artifacts makes even a physically rigid body appear to undergo non-rigid motion [JPipe2014]. However, motion tracking with vNavs when assuming rigid head motion has been shown to work [MDTisdall2012], and we assumed rigid-body motion in this study.

Susceptibility-induced non-rigidity of the head is less pronounced in the fetal head than in an actual person’s head. This is because susceptibility artifacts mainly arise from air/water susceptibility mismatches, and there is simply less air in the vicinity of the fetus’ head. Thus, we expect the rigidity assumptions used in prior studies with vNavs to be equally valid in the fetus.

**Volumetric Navigators (vNavs)**

The fact that only six degrees of freedom are needed to fully specify rigid body motion means that very little information is actually needed, relative to the typical amount of information contained in an MR image. For example, a 256x256x120 image (a typical MR image size) contains 256 · 256 · 120 = 7.86 · 10^6 numbers – one for each voxel. Since we only require six numbers to fully describe rigid motion, a typical MR acquisition contains vastly more information than is needed for motion tracking (by six orders of magnitude!)

On the contrary, volumetric navigators (vNavs) are fast, low-resolution, 3D echo-planar imaging (EPI) sequences that can be acquired in under a second [MDTisdall2012]. Unlike diagnostic MR sequences, vNav images do not show good anatomical or soft-tissue contrast. The acquisition calls for a very short TE (5-11ms) and very low flip angle (2-5 degrees), resulting in a primarily proton density-weighted image. In their initial work, Tisdall et al used a voxel size of 8x8x8mm³.

**Measuring Motion with vNavs**

In order to provide motion measurements of the object being imaged, vNavs acquired at successive time points need to be registered with a rigid-body registration tool. The result of such a registration is an affine transformation matrix with six independent parameters representing the six rigid-body degrees of freedom. By appropriately factoring such an affine transformation matrix, we can extract the values of these six motions along the six coordinate axes.

**Affine and Rigid Transformations**

A rigid-body transformation is an affine transformation, and in three dimensions can be represented by a 4x4 matrix with the following form:
Where we represent our three-dimensional coordinate \( \bar{x} = \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix} \) as a four-dimensional coordinate \( \bar{x}_{4D} \), such that:

\[
\bar{x}_{4D} = \begin{pmatrix} x \\ y \\ z \\ 1 \end{pmatrix}
\]

Thus, to obtain the transformed coordinate \( \bar{x}' \), we first take:

\[
\bar{x}'_{4D} = \begin{pmatrix} x' \\ y' \\ z' \\ 1 \end{pmatrix} = T\bar{x}_{4D}
\]

And then we define

\[
\bar{x}' = \begin{pmatrix} x' \\ y' \\ z' \end{pmatrix}
\]

In our definition of the transformation matrix \( T \), \( t_i \) is the translation of the origin of the original coordinate system along coordinate axis \( i \). \( R_{3D} \) is a three-dimensional rotation matrix.

**Extraction of Head Motion Parameters**

**Rotation Angles**

The three rotation angles are the three parameters that characterize \( R_{3D} \), the 3D rotation part of \( T \). Since \( R_{3D} \) is a 3D rotation matrix, it can be factored into three separate Givens Rotations, each of which describes a rotation about a single axis [GHGolub2012]. Of note is the fact that the Givens rotation matrices do not commute, and that the extracted rotation angles will depend on the order in which \( R_{3D} \) is factored into single-axis rotations. In this study, I chose the factorization \( R_{3D} = R_x R_y R_z \). Thus, as factored, the order of rotation is \( y \), then \( x \), then \( z \). This order was chosen because \( z \) was observed to typically have the largest rotation angles. Each matrix \( R_i \) is fully described by a single parameter, \( \theta_i \). For example:

\[
R_x = \begin{bmatrix}
\cos(\theta_x) & -\sin(\theta_x) & 0 \\
\sin(\theta_x) & \cos(\theta_x) & 0 \\
0 & 0 & 1
\end{bmatrix}
\]

By measuring the rotation angles \( \theta_i \) that are associated with each vNav registration, we can completely describe the rotational motion of the head.
Translations

It may seem that, since we already have the coordinate system origin translations from the parameters $t_x, t_y,$ and $t_z,$ that we do not need to do any more work in order to measure the translational motion of the fetal head. However, the absolute values of the translational coefficients $t_i$ describe the motion of the *origin of the coordinate system*, not the motion of the fetal head. In order to measure the translation of the fetal head, we need to measure the change in position of a point inside the head when transformed by the matrix $T$. That is, for a given point whose motion we wish to measure, $x_h,$ the translational motion $t_h$ is given by:

$$
\begin{pmatrix}
  t_h \\
  0
\end{pmatrix} = (T - I) \begin{pmatrix} x_h \\
  1 \end{pmatrix}
$$

$$
\begin{pmatrix}
  t_{h,x} \\
  t_{h,y} \\
  t_{h,z}
\end{pmatrix}
$$

In order to perform this, we first need to identify the point $x_h$ whose motion we wish to describe. These simple arithmetic manipulations allow for six physically meaningful quantities to be derived from each rigid-body registration.

**Issues in Using vNavs to Image the Fetus**

Imaging the fetus requires imaging the pregnant mother’s abdomen. As such, any acquired image that includes the fetal brain also includes much of the mother’s anatomy within the same field of view (FOV) (Figure 2.1). With the traditional vNav implementation, the unprocessed image contains only the head, so successive vNav acquisitions can be registered without any processing. However, this cannot be done in the fetus. We only wish to register images of the fetal head acquired at different time points, but our images contain mostly tissue from the mother. If we simply registered these unprocessed abdominal images to each other, the signal from the mother’s tissues would dominate the signal from the fetal head, and we would not measure the motion of the fetus.

The head of a fetus is smaller than that of an adult. This means that in order to obtain the same quality image of the fetal head for registering, we require a smaller voxel size. This, in turn, requires an increase in scan time, which reduces the temporal resolution for measuring the motion that we’re trying to detect.

In adults, the most important features for registering vNavs are the boundaries between brain, skull, subcutaneous fat, and air (Figure 2.2A). These are also the most significant edges in the entire image, which bodes well for simply registering entire vNav volumes to each other.

In fetal/abdominal imaging, fewer edges are associated with the fetal head. For instance, the fetal head is surrounded not by air, but by amniotic fluid, placenta, and maternal organs – all water-dense tissues. Thus, the boundary of the fetal head is much harder to discern, and certainly is not the only feature in the image (Figures 2.3B and 2.3C). Thus, segmentation of the fetal head is vital for motion tracking.
Identifying a Region-of-Interest (ROI) for Fetal Head Registration

As described, registration of vNav fetal head acquisition to another is unreliable due to the mother’s anatomy and the weak edges associated with the fetal skull. Thus, I identified a region with greater image contrast that provides more robust fetal head registrations.

The general region containing significant, robust image contrast is identified by the red line in Figure 2.3C. This region contains both the temporal lobe and cervical spinal cord (hyperintense regions) and the skull base (the dark, hypointense region). The red arrow, in particular, points out the skull base, which is dark due to its low proton density. It was observed that these regions do in fact move together with the fetal head, and thus that they are suitable for rigid-body registration to extract fetal head motion parameters.

Further, we note that in axial section (in the fetal anatomical coordinate system) the dark skull base regions have a characteristic “X” shape (Figure 2.2A). The “X”-shape appears reliable in fetal heads and provides edges in the axial plane that can be used for registration.
Figure 2.3: (A) vNav sagittal section of an adult brain. Acquisition voxel size was 8x8x8mm$^3$. Note the clear boundaries between brain, skull, air, and fat, as well as the lack of extraneous tissue in the image [Image from MDTisdall2012]. (B) vNav section (axial with respect to the mother) showing the fetal brain. Acquisition voxel size was 5x5x5mm$^3$. Note that the fetal brain only occupies a small portion of the image, and the edges defining it are less pronounced than those in the mother. Also, low-frequency coil sensitivity-related intensity variations are present in the image. (C) Same view as in (B), except now the image has been high-pass-filtered to remove coil sensitivity-related variations in intensity. The yellow dotted line encircles the fetal brain. The red dotted line highlights the high-contrast skullbase region suitable for registration. The red arrow points to the skull base region.
Part 3: Methods

Summary

Starting with already-acquired vNavs obtained from fetuses, I created ROI masks for the first time point, developed a registration pipeline to track the subsequent motion of that ROI, and extracted clinically-relevant motion parameters.

Data Used and Acquisition Parameters

Dedicated vNav Sequence

Data was acquired from 4 pregnant subjects on a Siemens 3T Trio system using a dedicated vNav sequence. This sequence consisted of fifty 3D vNavs acquired in succession with no other data recorded (TR=41ms, TE=13ms, 5x5x5mm³, FOV=300x300x120mm³, TA=738ms/volume, FA=5°). The total acquisition time for all 50 volumes was 39s. An example vNav obtained with this protocol is shown in Figure 2.4A.

HASTE-plus-vNav Sequence

One pregnant subject was scanned on a Siemens 3T Trio system using a HASTE+vNav sequence. In this sequence, a twenty-slice Half-fourier Acquisition Single-shot Turbo spin-Echo (HASTE) image was acquired. HASTE is a slice-by-slice acquisition that involves a 90º excitation pulse followed by a TSE readout that acquires the data for a full slice (hence, “Single-shot”). However, because it requires T₂ relaxation to achieve the desired image contrast, and because TSE is a SAR-intensive process, a long TR is needed between slices. Between the end of one readout and the start of the next excitation, 1.2 seconds pass where nothing happens. Instead of just wasting that time, however, a vNav volume can be acquired.

In this sequence, twenty HASTE slice acquisitions were each followed by a vNav volume (TR=41ms, TE=13ms, 5x5x5mm³, FOV=300x300x120mm³, TA=738ms/volume, FA=5°). Previously, we began to acquire a new vNav as soon as we had finished acquiring the previous one, thus the temporal resolution of the vNavs was equal to the TA: 738ms. In this case, however, we can only acquire a vNav once per HASTE slice. This results in vNavs being acquired with a temporal resolution of approximately one per 1.5 seconds.

Because these vNavs were acquired immediately following a HASTE slice acquisition, and because HASTE uses a large tip angle for its excitation pulse, the signal from the region of where the slice was acquired is significantly reduced. Put another way, all of the available magnetization in this slice was used for the HASTE acquisition, and we did not wait long enough for this magnetization to fully relax before acquiring the vNav volume. The result is an artifact in the vNavs (Figure 2.4B).

Image Preprocessing
In images acquired from both the dedicated vNav sequence and from the HASTE/vNav sequence, I wanted to first process the images to remove as many artifacts as possible.

**Image Normalizing**

In all images, coil sensitivity artifacts were observed. This meant that, on top of the visible anatomical detail in the image, there was a slowly-varying intensity pattern due solely to the spatial sensitivities of the receive coils used in imaging. Additionally, because vNavs involve 3D imaging (i.e., they used non-slice-selective excitation pulses and two phase encode directions) and a short TR and small flip angle, it took many repetitions before the baseline image intensity reached a steady-state value. Thus, in the vNavs acquired early in the 50-vNav sequence, there is simply more signal at all locations. It was desired to remove this temporal intensity variation prior to registration.

This was done by smoothing each 3D volume with a Gaussian filter, and then dividing the original image by this “smoothed” image. For the dedicated vNav sequence volumes, an isotropic blur kernel was used to give a normalized image (Figure 2.5A). However, to account for the planar artifact in the HASTE/vNav sequence, an anisotropic blur kernel was used for those volumes. The kernel was chosen to be much large in the plane of the HASTE artifact, which removed the unnatural edges associated with the spin history effect (Figure 2.5B).

**ROI Mask Creation**
I needed a rigid, high-contrast volume associated with the fetal heat for each time series of vNav volumes. I obtained this ROI by manually creating a mask for the first mask in each time series. I also created masks of particularly high-contrast image features to further aid in the registration.

**Head ROI Masking**

An example head ROI is shown in Figure 2.6A and 2.6B. In this picture, all voxels within the illustrated boundary are part of the binary ROI mask. Note that while rigidly affixed to the entire fetal head, only the lower cranium is identified for purposes of registration.

**High-Contrast Feature ROI Masking**

Registration tools often allow the user to provide additional masks for weighting different spatial regions more than others when calculating the value of the objective function. I used this capability to provide additional weighting for a smaller ROI consisting of the highest-contrast areas of the mask in Figure 2.6A. This high-contrast ROI mask is shown in Figure 2.6C and 2.6D.

Figure 2.6: (A) Coronal section of "head ROI" mask (B) axial section of "head ROI" mask (C) coronal section of "high-contrast ROI" mask (D) axial section of "high-contrast ROI" mask
Registration Pipeline and Parameter Extraction

For each series of vNavs, I created these masks only for the volume at the first time point. In order to avoid having to repeat this same process twenty or fifty times, I developed an automated pipeline that used just these two masks, along with the original vNav images, to obtain transformation matrices for all time steps. The operation of this pipeline is illustrated in Figure 2.7. There are two important operation principles for this pipeline.

First, we assume that, from one measurement to the next, the fetus’ head does not move very much. This seems reasonable, given that the fetus is constrained, and that the mother does not move. Based on our vNav data, this is empirically true as well. The low-motion assumption is valuable because, if we know the position of the head at time point n, it means the head’s position at time point n + 1 is very close. Knowledge of the head position at time point n is manifested in the ROI mask at that time point – if we have an accurate mask, then we necessarily know where the head is. If we dilate this ROI mask, we obtain a mask for all of the voxels nearby, plus the original ROI. Since we are assuming that there is little head motion, it is implicit that, at time point n + 1, the head will still be “nearby.” Thus, this dilated ROI mask provides a reasonable “search area” in which we will likely find the head at time point n + 1. By applying this mask to the whole vNav volume at time point n + 1, we can automatically remove most of the unwanted signal associated with maternal anatomical structures! Once this is done, the main obstacle to successful registration is removed, and we can register the vNavs from the two time points together.

Secondly, we note that, once we have successfully registered the vNav from one time point (time point...
to the vNav at the next time point (time point $n + 1$), we have the affine transformation from time point $n$ to time point $n + 1$. By applying this transformation to all ROI masks at time point $n$, we will obtain masks for the exact same structures that are aligned with the image at time point $n + 1$.

In summary, the first observation enables us to register the volume from one time point to that at the next time point, assuming with have the proper ROI masks for the first time point volume. Once we have done this, the second observation tells us we can create the proper ROI masks, for that next time point. Taken together, they create an iterative method whereby one successful registration leads directly to another. As with any inductive process, we only need to provide the “starting masks” for the first time point. These are exactly the masks that were manually produced in the previous section.

**Registration Pipeline Stages**

1. **Mask Dilation**: Here, the previously-known mask is simply dilated. This provides a zeroth-order estimate of the ROI in the next time point – the one to which we are registering the current image.

2. **Apply Masks**: We multiply the high-pass-filtered images taken at times $t_n$ and $t_{n+1}$ by the respective masks. This removes most of the maternal tissue from the image and prepares the images for registration.

3. **Image Registration**: The masked images ideally contain only the fetal head ROI. These images are registered with the FSL FLIRT registration tool [MJenkinson2001, MJenkinson2002], using the high-contrast region ROI masks previously described. The output of this stage is a rigid-body transformation matrix describing the motion from one time point to the next.

4. **Apply Transformation to Original ROI Mask**: Now that we know the motion from time point $t_n$ to time point $t_{n+1}$, we can transform the original ROI mask so that it’s precisely aligned with the ROI at time $t_{n+1}$. Thus, starting with the $t_n$ ROI mask, we were able to successfully generate the $t_n$ to $t_{n+1}$ affine transformation matrix and the $t_{n+1}$ ROI mask. We can apply the exact same steps to obtain the transformation matrices and ROI masks for all subsequent time points.

**Ascertaining Whether a Registration Is Successful**

Unfortunately, there is no “ground truth” of motion for automatically determining when the registration in step (3) of the pipeline was successful, and when it failed. For this analysis, I visually compared each transformed 3D volume with the volume that it was supposed to be registered to. Doing this, I could identify when a registration was a failure – the images were visible misaligned.

If the images appeared properly registered, however, I could not quantify how accurately aligned they were. This would require some way of more precisely measuring motion over the same time for use as a “ground truth,” and we did not have such data.
**Part 4: Results**

*Motion Measurements from Dedicated vNav Sequence*

Figures 2.8 through 2.11 show plots of motion along the six coordinate axes for the four fetuses imaged with the dedicated vNav protocol. Figure 2.12 has plots of position along all six coordinates for the one HASTE+vNav data set.

*Registration Performance*

*FLIRT Registration Success Rate*

As shown in Figures 2.9 through 2.11, the FLIRT registration was always successful when the motion of the fetus was low. In these cases, the dominant source of fetal motion was the breathing of the mother. This is apparent from the periodic nature of many of the coordinates’ time series.

When there was significant fetal motion, FLIRT was not always successful. In Figure 2.8, FLIRT was successfully able to detect angular excursions of more than 80 degrees, but the registration was still not always successful. With this data set, the registration worked 40 out of 49 times (82%). In Figure 2.12, the motion was not so extreme, but translation excursions were still greater than 7mm, and rotational excursions were greater than 15 degrees. In this case, registration only failed once, for a success rate of 95%.

*Registration Run Time*

As currently implemented, registration of one vNav to another, including all the overhead of updating masks, takes between 9.8 and 10.7 seconds. Thus, registration of a stack of 50 vNavs, which requires 49 separate registrations, takes from 478 to 522 seconds.
Figure 2.8: Head images and motion measurements for subject 1 scanned with the dedicated vNav sequence (A) axial view of fetal head (B) coronal view of fetal head (C) time-series plots of extracted head rotation parameters (D) time-series plots of extracted translational motion of head center. Gray background areas represent time points for which the registration failed and no reliable motion data was obtained.
Figure 2.9: Head images and motion measurements for subject Z scanned with the dedicated vNav sequence (A) coronal view of fetal head (B) oblique sagittal view of fetal head (C) time-series plots of extracted head rotation parameters (D) time-series plots of extracted translational motion of head center
Figure 2.10: Head images and motion measurements for subject 3 scanned with the dedicated vNav sequence (A) coronal view of fetal head (B) oblique sagittal view of fetal head (C) time-series plots of extracted head rotation parameters (D) time-series plots of extracted translational motion of head center.
Figure 2.11: Head images and motion measurements for subject 4 scanned with the dedicated vNav sequence (A) axial view of fetal head (B) oblique coronal view of fetal head (C) time-series plots of extracted head rotation parameters (D) time-series plots of extracted translational motion of head center.
Figure 2.12: Head images and motion measurements for subject 1 scanned with the HASTE/vNav sequence (A) axial view of fetal head (B) coronal view of fetal head (C) time-series plots of extracted head rotation parameters (D) time-series plots of extracted translational motion of head center. Gray background region in plots denotes time for which no accurate motion data was measured due to poor registration.
Part 5: Discussion

vNavs Can Accurately Measure Fetal Head Motion

By successfully registering one volume to the next, I have successfully shown that vNavs can be used to accurately track the motion of the fetal head. This by itself is significant – it means that, within the uterus, there is sufficient image contrast in a low-flip, short-TR sequence for the fetal head to be identified and aligned.

Additionally, I have shown that vNavs embedded in a clinical HASTE sequence can be used to obtain the same precise fetal head motion tracking. This result goes one step further in illustrating the potential for vNavs to be used for motion tracking in clinical MRI.

Automated Segmentation and Faster Registration are Needed

While I have shown that vNavs can be used to measure fetal motion, and have obtained quantitative results illustrating such, there are still several hurdles to clinical relevance that need to be overcome. Both ultimately relate to the need for fast, automatic motion tracking for prospective motion correction.

Automated Segmentation

While the iterative registration pipeline developed for this work eliminates the need for manually segmenting an ROI at each time point, it still requires a manually-created mask to begin the process. Creating this mask takes time, and is altogether unacceptable for real-time motion correction. Fast, automatic segmentation will require additional work, and might be accomplished by template/pattern matching. This may be aided by identifying a 3D rectangular region of interest to perform the initial template matching. Identification of this ROI would be exactly the same as identifying the imaging volume before any MR acquisition, and would not likely prove an impediment to clinical use.

Fast Registration

The original work on volumetric navigators was able to perform prospective motion correction because the entire volume acquisition and registration process took under 500ms [MDTisdal2012]. Since this was embedded in a clinical sequence with a TR of longer than this, it was possible to obtain current motion parameters at each TR interval. As current described, fetal motion tracking with vNavs takes 10 seconds to perform this same registration – completely unacceptable for real-time motion correction. Thus, future work will need to perform these registrations faster in order for vNav-based motion correction to be a viable option in fetal MR imaging.
Part 6: Conclusion

I have demonstrated that volumetric navigators (vNavs) can be used in fetal MRI to accurately measure motion with a time resolution of under one second. By measuring fetal motion from vNavs which were embedded in a clinical sequence, I have also demonstrated that motion tracking can be performed under realistic imaging constraints. These results strongly suggest that vNavs will enable prospective motion correction in fetal imaging, and that they will prove a valuable clinical contribution. I have also discussed several limitations of the current implementation as a means of prospectively correcting for fetal motion in a clinical sequence, and have outlined the next steps needed to overcome these limitations.
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Chapter 3
Physical Realization of a Novel Technique to Decouple Parallel Transmit (pTx) Coil Arrays for 7-Tesla MRI

Part 1: Introduction

Parallel Transmission (pTx) in MRI can lead to greater spatial uniformity in B1 profiles and reduced specific absorption rate (SAR) by using multiple spatially-orthogonal coils for RF excitation. [YZhu2002, KSetsompop2006, KGuérin2014] It is particularly relevant to 7-Tesla MRI, where these two considerations are limiting factors on the ability to design RF pulses. pTx, rather than use a single coil with one degree of freedom for RF excitation, uses an array of independent coils, each one a separate degree of freedom.

However, with any multiport network, coupling between pTx coil elements leads to back-reflected power, reducing the efficiency of the pTx system. Thus, there is a need for efficient methods of decoupling elements in pTx arrays to improve RF power efficiency.

Existing techniques to decouple elements in a pTx array include overlapping the coil loops by a critical amount [PBRoemer1990] and using capacitive or inductive decoupling [JWang1996]. However, these techniques only work to decoupling nearest-neighbor coil elements. In a general pTx coil, there may be significant coupling between non-nearest-neighbor coils. It has been proposed to use active elements in decoupling network [PPStang2011]. However, there is still a need for a robust, passive network to decouple general pTx coil arrays.

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Part 2: Theory

A method for decoupling pTx channels with a *decoupling matrix* has been proposed [ZMahmood2013, ZMahmood2014]. The proposed decoupling matrix diagonalizes the impedance matrix of the pTx coil array, and matches each diagonal element to the output of the corresponding RF power amplifier. The diagonalization of the impedance matrix is accomplished in hardware with a novel technique using hybrid ring couplers. The theoretical description of the decoupling matrix that follows is based on previous work in [WPGeren1996, ZMahmood2013, ZMahmood2014].

Z- and S-parameters as Descriptions of Multiport Networks

Linear, multi-port networks can be described by a complex-valued matrix. Two common matrices used to describe such a network are the impedance matrix (the Z-matrix) and the S-parameter matrix (the S-matrix).

A Z-parameter matrix element \( Z_{ij} \) is defined as the voltage measured on port \( i \) divided by the current injected into port \( j \), when all ports are open-terminated. If \( Z_{ij} = 0 \) for all \( i \neq j \), then the network is fully decoupled, since current injected on one port does not affect the voltage on any other ports. This is equivalent to the Z-matrix being a diagonal matrix. A scalar impedance \( Z \) can be expressed as the sum of a real resistance and an imaginary reactance: \( Z = R + jX \). Likewise, and impedance matrix can be expressed as the sum of a resistance matrix and a reactance matrix, where each element \( Z_{ij} = R_{ij} + jX_{ij} \).

An S-parameter matrix contains the same information about a network as the Z-matrix. However, the measurement conditions for each parameter are different from those for a Z-matrix. While a Z-matrix measures the voltage-to-current ratio when each port is open, the S-parameter matrix measures the ratios of the propagating voltage/current power waves at each port, when each port is terminated by a characteristic reference impedance. This is illustrated in Figure 3.1, where \( a \) is the incident power wave, and \( b \) is the reflected power wave. For each port \( i \), we define that port’s reference impedance to be \( Z_{0i} \). In our case, the reference impedance is 50Ω for all ports.

The principal advantage of using S-parameters over using Z-parameters is in the ease of measurement. S-parameters can be measured by connecting a port to a network analyzer with a cable whose characteristic impedance is the reference impedance of measurement,

\[
b = S_c a
\]

Figure 3.1: Illustration of S-matrix for an n-port network. The incident power wave is \( a \) and the reflected power wave is \( b \). The n-port pTx array is described by the S-matrix \( S_c \).
while accurately terminating ports with an open circuit to measure Z-parameters is difficult in practice [THLee2004].

Both the Z- and S-matrices provide a complete description of the network, and it is straightforward to extract one set of parameters from the other. Using our 50Ω reference impedance for all ports, the relation between the Z-matrix and the S-matrix is [PRusser2006]:

\[
Z = g(I - S)^{-1}(I + S)g
\]

Here, \(S\) is the S-matrix, \(I\) is the identity, and \(g\) is defined as:

\[
g = \begin{pmatrix}
\sqrt{Z_{01}} & \cdots & 0 \\
\vdots & \ddots & \vdots \\
0 & \cdots & \sqrt{Z_{0n}}
\end{pmatrix}
= \begin{pmatrix}
\sqrt{50} & \cdots & 0 \\
\vdots & \ddots & \vdots \\
0 & \cdots & \sqrt{50}
\end{pmatrix}
\]

It is noted that this is simply a generalized matrix formulation for the scalar equivalent of this equation – that which relates a scalar impedance mismatch to the transmission and reflection coefficients.

**Interconnection of Two Multiport Networks – S-parameters**

Suppose we connect an n-port network and a 2n-port network as shown in Figure 3.2. If we design the S-matrix of the 2n-port network to be as shown, then the resulting N-port S-matrix looking into the composite network will be as shown. Specifically, we will have:

\[
S_{Ac} = AS_cA^T
\]

**Properties of Passive Multiport Networks**

A pTx coil array is a passive, reciprocal network as it consists entirely of capacitive, inductive and resistive elements [PChirlian1969]. Such a network has both a symmetric Z-matrix and a symmetric S-
matrix [PRusser2006]. That a network has a symmetric impedance matrix means both its resistance and reactance matrices are also symmetric. As both are defined as real matrices, this means that both are Hermitian, and that their eigenvectors are orthogonal.

As an application of this, suppose we wish to diagonalize the reactance matrix $X$ into $\Lambda_X$. Then, we require a multiplication by $V_X$, the matrix whose columns are the eigenvectors of $X$:

$$\Lambda_X = V_X^{-1} X V_X$$

Since $X$ is a real, symmetric matrix, $V_X$ is a real orthogonal matrix. As it is orthogonal, it is also unitary, i.e.:

$$V_X^T = V_X^{-1}$$

This means that the reactance matrix $X$ is diagonalized by a unitary matrix via:

$$\Lambda_X = V_X^T X V_X$$

**Interconnection of Two Multiport Networks – Z-parameters**

We can also derive the impedance matrix of a composite network by noting the relationship between the $S$ and $Z$ matrices:

$$Z = g(I - S)^{-1}(I + S)g$$

We have shown that inserting a $2n$-port network with the illustrated block form transforms the $S$-matrix via:

$$S_A = ASA^T$$

Here, motivated by the fact that we are dealing with a passive network, we make the additional crucial assumption that $A$ is a unitary matrix. This implies:

$$Z_A = g(I - S_A)^{-1}(I + S_A)g$$

$$= g(A1AT - ASA^T)^{-1}(A1AT + ASA^T)g$$

$$= g A(I - S)^{-1} A^T A(I + S) A^T g$$

$$= Ag(I - S)^{-1} (I + S) g A^T$$

$$= AZA^T$$

In the last step, we exploited the fact that $g$ is just $\sqrt{50} \cdot I$ in our case. This is an important result: it implies that for a unitary $A$ in the $S$-matrix shown in Figure 3.2, the $2n$-port network will transform both the $Z$- and $S$-matrices as shown.

**Diagonalization of the Reactance Matrix X**

Suppose we let $A = V_X^T$, the matrix whose rows are the eigenvectors $X$. Then, the network in FIGN2NCONNECT will diagonalize $X$ when it transforms $Z$:
Removal of the Reactance Matrix $X$

Suppose we insert a reactive element in series with port $P_1$. When we do this, we will effectively be adding this reactance to the $Z_{11}$ component of the $Z$-matrix. However, this series reactance will not affect any other $Z$-parameters, since it will not affect the “test current” injected into the network.

Taking advantage of this, we can add a series reactance to each port of the network, such that the series reactance on port $i$ is equal to $-A_{X,ii}$. The impedance matrix will then be:

$$Z_{ser} = Z_A - jA_X$$

$$= V_X^T R V_X + jV_X^T X V_X$$

Since $R$ and $V_X$ are both real matrices, $Z_{ser}$ is now a real matrix. We have completely removed all reactance!

Diagonalization and Matching of the Resistance Matrix

We have demonstrated how, with a 2n-port network as shown in Figure 3.2, and with $A$ being a unitary matrix, we can diagonalize a reactance matrix. Since the resistance matrix is also symmetric and real, its eigenvector matrix is also unitary. We can therefore use the same architecture to diagonalize the resistive matrix $Z_{ser}$ obtained from the last section.

At this point, however, we do not wish to remove the residual diagonal resistance. Rather, we wish to match it to the output resistance of the n radio-frequency power amplifiers that drive the pTx coil array. This is easy to do at this point – since we have removed all reactance, and have diagonalized the resistance matrix, $Z$ is now diagonal. This implies that all ports are fully decoupled, and that we can match each individual port to the individual 50Ω power amplifier output via a single-port matching network.

Physical Implementation of the Unitary Transformation

In order to implement a decoupling matrix, it is necessary to physically implement a 2n-port network with an S-parameter matrix given by:

$$S_A = \begin{bmatrix} 0 & A \\ A^T & 0 \end{bmatrix}$$

It was first noted that an orthogonal matrix such as $A$ can be decomposed into $\frac{n(n-1)}{2}$ Givens rotation matrices [GHGolub2012]:
\[
A = R_{12}R_{13}R_{14} \ldots R_{1n}R_{23}R_{24} \ldots R_{2n}R_{34} \ldots R_{n-1,n}
\]

\[
= \prod_{i>0}^{i \leq n-1} \prod_{j>i}^{j \leq n} R_{ij}
\]

Each \(R_{ij}\) has the form:

\[
R_{ij} = \begin{bmatrix}
1 & \cdots & 0 & \cdots & 0 & \cdots & 0 \\
\vdots & \ddots & \vdots & \ddots & \vdots & \ddots & \vdots \\
0 & \cdots & \cos(\theta) & \cdots & -\sin(\theta) & \cdots & 0 \\
\vdots & \vdots & \ddots & \ddots & \ddots & \ddots & \vdots \\
0 & \cdots & \sin(\theta) & \cdots & \cos(\theta) & \cdots & 0 \\
\vdots & \vdots & \vdots & \ddots & \ddots & \ddots & \vdots \\
0 & \cdots & 0 & \cdots & 0 & \cdots & 1
\end{bmatrix}
\]

Matrix \(R_{ij}\) is simply an identity matrix, except for the 2x2 submatrix comprising in the intersection of rows \(i\) and \(j\) with columns \(i\) and \(j\). This 2x2 submatrix is a rotation matrix with rotation angle \(\theta\). We can therefore represent an arbitrary unitary transformation matrix as a series of independent rotations, each specified by a single angle.

Suppose we define \(S_A\) such that:

\[
S_A = S_{AR} = S_{R12}S_{R13} \ldots S_{Rn-1,n}
\]

Where

\[
S_{Rij} = \begin{bmatrix}
0 & R_{ij} \\
R_{ij}^T & 0
\end{bmatrix}
\]

If we connect a 2n-port network with S-matrix \(S_A\) together with an n-port network with S-matrix \(S_C\) as shown in figure FIGN2NCONNECT, then we will find:

\[
S_{AC} = R_{12}R_{13} \ldots R_{n-1,n}S_C R_{n-1,n}^T \ldots R_{13}^T R_{12}^T
\]

\[
= AS_C A^T
\]

Thus, we can implement a decoupling matrix with a network whose S-matrix has the form of \(S_{AR}\).
It was previously observed [ZMahmood2014] that an asymmetrical 180-degree hybrid ring coupler can implement, in hardware, the matrix $S_{R_{ij}}$ for arbitrary rotation angle.

**Deriving the S-parameters**

Consider the device shown in figure 3.3. This figure shows a hardware implementation of $S_{R_{12}}$ using a transmission line hybrid coupler. The hybrid ring coupler consists of four sections of transmission line: two of characteristic impedance $Z_{0B}$ and electrical length $\frac{\lambda}{4}$, one of characteristic impedance $Z_{0A}$ and electrical length $\frac{\lambda}{4}$, and one of characteristic impedance $Z_{0A}$ and electrical length $\frac{3\lambda}{4}$. We define ports $P_3$ through $P_n$ to be coincident with ports $P_{3+n}$ through $P_{2n}$, respectively. We define $Z_{0A}$ and $Z_{0B}$ in terms of a parameter $\theta$, such that:

$$Z_{0A} = 50\Omega \cdot \frac{1 + \gamma}{\sqrt{1 + \gamma}}$$

$$Z_{0B} = 50\Omega \cdot \sqrt{1 + \gamma}$$

$$\gamma = \left(\frac{\sin \theta}{\cos \theta}\right)^2$$

Figure 3.3: A hardware implementation of S-parameter matrix $S_{R_{ij}}$. There is no coupling between any two of ports $P_3$ through $P_n$ or $P_{3+n}$ through $P_{2n}$.
We note that, for \( i \neq \{1,2\}, S_{i,i+n} = S_{i+n,i} = 1 \), since port \( P_i \) is at the same location as port \( P_{i+n} \). We also note that, for \( j \neq i \pm n \), \( S_{ij} = S_{ij} = 0 \).

**Deriving \( S_{12} \)**

By symmetry, \( S_{12} = S_{21} = 0 \) and \( S_{1+n,2+n} = S_{2+n,1+n} = 0 \). We can show this, without loss of generality, by considering what happens to a power wave injected into port \( P_1 \). This power wave of normalized amplitude will be split into two power waves, one of which travels along the “top” half of the ring (i.e. towards \( P_{2+n} \)), while the other travels along the “bottom” half. A portion of that on the “top” half will be coupled out of the ring via \( P_{2+n} \) and a portion of that on the “bottom” half will be coupled out via \( P_{1+n} \). Those portions remaining in the ring will travel to \( P_2 \). At this point, the amplitudes of the traveling waves are defined as \( A_t \), for the “top” travelling wave, and \( A_b \) for the “bottom”. Since the “bottom” wave will have travelled an extra half-wavelength, it will have the opposite phase from the “top” wave. Thus, the combined amplitude at \( P_2 \) will be \( A_b - A_t \).

By the reciprocity of this passive network, an injected normalized power wave at port \( P_2 \) must yield the same amplitude at \( P_1 \) as this. In this case, however, the “top” travelling wave has the same amplitude as the “bottom” traveling wave of the previous case. Therefore, the overall amplitude at \( P_1 \) will be \( A_t - A_b \). This can only be equal to \( A_b - A_t \) if \( A_b = A_t \).

This implies that no power injected at port \( P_1 \) is ejected at \( P_2 \). This is equivalent to saying that \( S_{12} = S_{21} = 0 \). The same argument shows that \( S_{1+n,2+n} = S_{2+n,1+n} = 0 \).

**Deriving \( S_{1,1+n} \)**

Because we know that no power injected into \( P_1 \) will appear at \( P_2 \), we can simplify the topology of the hybrid ring coupler when looking into port \( P_1 \). This simplification is shown in Figure 3.4.

The resulting equivalent circuit is simply a parallel combination of two quarter-wave impedance transformers. The impedance looking into the \( Z_{0B} \) section is:

\[
Z_{B,in} = \frac{Z_{0B}}{50\Omega}
\]

\[
= 50\Omega \cdot (1 + \gamma)
\]

Similarly, the impedance looking into the \( Z_{0A} \) section is:

\[
Z_{A,in} = 50\Omega \cdot \frac{1 + \gamma}{\gamma}
\]

The fraction of the power that down the \( Z_{0B} \) section, towards \( P_{1+n} \), is precisely \( S_{1,1+n}^2 \). Given that \( Z_{B,in} \) and \( Z_{A,in} \) are connected in parallel, this quantity is:

\[
|S_{1,1+n}| = \sqrt{\frac{Z_{B,in}}{Z_{B,in} + Z_{A,in}}}
\]
Similarly, it can be shown that:

\[
\left| S_{1,2+n} \right| = \cos(\theta)
\]

By the symmetry of the hybrid ring coupler, we also observe that \( S_{1,2+n} = -S_{2,1+n} \) and \( S_{2,2+n} = S_{1,1+n} \).

Finally, we need to find the phase of the S-parameters. Since the electrical length from \( P_1 \) to \( P_{1+n} \) is a quarter wavelength, this S-parameter will have -90 degrees of phase. This is equivalent to a multiplication of its magnitude by \(-j\), giving: \( S_{1,1+n} = -j \cdot \sin(\theta)\). However, we can remove this phase by adding a 270-degree electrical length path to port \( P_1 \). This will give the path from \( P_1 \) to \( P_{1+n} \) 360 degrees of phase, giving \( S_{1,1+n} = \sin(\theta) \). Doing likewise for port \( P_2 \) gives all nonzero S-parameters a full 360 degrees of phase. As we will discuss, this 270-degree path is subsumed into the coaxial cable connection from one hybrid ring to another.

*Entire Matrix Form for S*
Combining all the previous derivations, we find the following $S$-parameter matrix for the circuit in Figure 3.3:

\[
S = \begin{bmatrix}
0 & \cdots & \cdots & \cdots & 0 & \sin(\theta) & \cos(\theta) & 0 & \cdots & 0 \\
\vdots & \ddots & \ddots & \ddots & \cdots & -\cos(\theta) & \sin(\theta) & 0 & \cdots & 0 \\
\vdots & \ddots & \ddots & \ddots & \cdots & 0 & 0 & 1 & \vdots \\
\vdots & \ddots & \ddots & \ddots & \cdots & \vdots & \vdots & \ddots & \vdots \\
0 & \cdots & \cdots & \cdots & 0 & 0 & 0 & \cdots & \cdots & 1 \\
\sin(\theta) & -\cos(\theta) & 0 & \cdots & 0 & 0 & \cdots & \cdots & 0 \\
\cos(\theta) & \sin(\theta) & 0 & \cdots & 0 & \vdots & \ddots & \vdots & \vdots \\
0 & 0 & 1 & \vdots & \vdots & \ddots & \ddots & \vdots & \vdots \\
\vdots & \ddots & \ddots & \ddots & \cdots & \vdots & \vdots & \ddots & \vdots \\
0 & 0 & \cdots & \cdots & 1 & 0 & \cdots & \cdots & 0
\end{bmatrix}
\]

This is precisely the form of $S_{R12}$ as defined in the previous section. Thus, a transmission line hybrid ring coupler can implement a Givens rotation, and a properly designed network of hybrid ring couplers can implement a unitary transformation $A$, as required for a decoupling matrix.

**Impedance Matching at the Inputs**

The $S$-matrix we have derived for this circuit has all zeros on the main diagonal, meaning that no power injected at any port is reflected back to that same port. Thus, this hybrid coupler must have perfect impedance matching at each input port, and the input impedance at all ports must equal 50Ω.

We can prove this using the equivalent circuit in Figure 3.4. The input impedance is the parallel combination of $Z_{B, in} = 50\Omega \cdot (1 + \gamma)$ and $Z_{A, in} = 50\Omega \cdot \frac{1 + \gamma}{\gamma}$. Calculating the overall input impedance:

\[
Z_{in} = Z_{B, in} || Z_{A, in} \\
= 50\Omega \cdot \frac{(1 + \gamma)(1 + \gamma)}{\gamma \cdot \left(1 + \gamma + \frac{1 + \gamma}{\gamma}\right)} \\
= 50\Omega \cdot \frac{1 + \gamma}{\gamma \cdot \left(1 + \frac{1}{\gamma}\right)} \\
= 50\Omega
\]

Thus, we will have perfect impedance matching at all ports.
Implementation of Givens Rotations of Arbitrary Size

While the relationship between rotation angle and hybrid ring coupler characteristic impedances is correct, the physical constraint that the characteristic impedance be positive limits the range of valid rotation angles to between 0° and −90°. However, by inserting an additional 180° of phase in the electrical path before $P_1$ and/or $P_2$, we can implement the full range of rotations.

As an illustration of this principle, consider the default rotation matrix using the implementation described above:

$$ R(\theta) = \begin{bmatrix} 
\sin(\theta) & \cos(\theta) & \cdots & 0 \\
-\cos(\theta) & \sin(\theta) & \cdots & 0 \\
\vdots & \vdots & \ddots & \vdots \\
0 & 0 & \cdots & 1 
\end{bmatrix} $$

Suppose we insert an extra 180° of phase at the inputs to both $P_1$ and $P_2$. This will give the following rotation matrix:

$$ R_2(\theta) = \begin{bmatrix} 
-\sin(\theta) & -\cos(\theta) & \cdots & 0 \\
\cos(\theta) & -\sin(\theta) & \cdots & 0 \\
\vdots & \vdots & \ddots & \vdots \\
0 & 0 & \cdots & 1 
\end{bmatrix} $$

We now note that

$$ R_2(\theta) = R(\theta + 180°) $$

This means that, by adding 180 degrees of phase to each path, we have effectively changed the range of valid Givens rotations to between 90° and 180°. Similar strategies, combined with permuting the inputs to the hybrid coupler, enable any Givens rotation to be implemented with this approach.
Part 3: Methods

The decoupling matrix has previously been validated theoretically, but a physical realization had been limited to a simple 2-channel pTx coil. This example only decoupled a pair of physically adjacent coil elements, and such a system can be easily decoupled by other means [JWang1996]. Thus, the main advantage of the decoupling matrix – its ability to decouple arbitrarily many coil pairs without concern for physical geometry – was not shown in this demonstration.

My work involved building a physical decoupling matrix for a 4-channel pTx coil array using the automated design tools previously developed [ZMahmood2015].

pTx Coil Characterization

Design of the decoupling matrix requires knowing the S-parameters of the coil array it will work with. The first step my work thus to obtain reliable S-parameters for my coil. For this project, I wished to show that the decoupling matrix strategy could be used to eliminate coupling between next-nearest neighbor coil elements. This required that in its fully-coupled state, there was normally significant coupling between these coil elements.

Choice of pTx Coil

For the previous 2-channel decoupling matrix demonstration, a 4-channel pTx coil had already been built, shown in Figure 3.5B. I used this coil for the design and demonstration of the 4-channel decoupling matrix.

Measurement Setup

In order to assess the performance of the decoupling matrix, I needed to ensure that the coil setup was as repeatable as possible. If it weren’t, then it wouldn’t be possible to tell if poor decoupling were due to the decoupling matrix not working, or due to the nature of the pTx coil having changed. Changes in the measured S-parameters of the pTx coil array arise because of changes in coil loading conditions. This could be due to different placement of the coil within the RF shield, or due to a different placement of the loading phantom within the bore.

To eliminate these sources of error, I built a jig that was rigidly affixed to the coil, the loading phantom, and the bore simulator/RF shield. Additionally, the location of the bore simulator and network analyzer was not changed relative to lab benches, etc. for the duration of this experiment. Figure 3.5A shows the exterior of the bore simulator/RF shield in relation to the lab. Figure 3.5B shows the interior of the bore simulator, including the pTx coil, loading phantom, and repeatability jig.

Loading Phantoms
A loading phantom was placed within the coil during all S-parameter measurements. This ensured greater repeatability in the S-parameter measurements, and more-accurately simulated the effects of a human head being placed inside the coil. Three loading phantoms were used in total, and all are shown in Figure 3.6. In order to obtain the S-parameters for decoupling matrix design, a 1600mL loading phantom was used. All phantoms were water doped with NaCl and Gadolinium to approximate the electrical conductivity, permittivity, and NMR relaxation times of human tissue.

**Design of the Decoupling Matrix**

Previous work on the decoupling matrix concept was focused on automating its design given a measurement of pTx coil S-parameters [ZMahmood2013, ZMahmood2014]. Thus, once I had the coil S-parameters, I simply used existing MATLAB code to automatically generate all the necessary Givens

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Figure 3.5: (a) Test bench showing bore simulator/RF shield, 4-channel network analyzer, and decoupling matrix. (b) Close-up of loading phantom, pTx coil, jig, and interior of bore simulator. All S-parameter measurements involving the pTx coil were taken under precisely these test conditions. The jig was made of ABS plastic, and did not load the coil.

Figure 3.6: (i) 1600mL loading phantom (used for design) (ii) 2000mL loading phantom (iii) 2700mL loading phantom
rotation angles for this decoupling matrix.

**Building the Microstrip Boards**

The Larmor frequency for 7-Tesla MRI is 297.2MHz, so the operation and tuning frequency for all electronics needs to be precisely this value. This dictates the necessary lengths of all traces in our microstrip PCB layouts.

**Choice of Substrate**

We used 59mil (1.5mm) Rogers 3003 substrate to manufacture our microstrip layouts. The thickness of the copper cladding on both sides was 1.4mil (35.6um). The previous realization of a decoupling matrix used an FR-4 substrate, but this has a significant loss tangent at 300MHz. Rogers 3003 is constructed of a Teflon-based substrate, and possess a loss tangent that is an order of magnitude lower than that of FR-

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**Figure 3.7:** (A) Previous EAGLE layout of microstrip hybrid ring coupler for 59mil Rogers 3003 substrate. (B) Compressed, improved layout. Both of these layouts were generated automatically using a MATLAB script that creates EAGLE *.brd files from the desired Givens rotation angle.
In principle, it is possible to make a microstrip transmission line with any characteristic impedance ($Z_0$) simply by choosing the appropriate copper trace width ($w$). Analytical, empirical equations have been published that relate $Z_0$ and $w$. Additional needed parameters are the substrate dielectric ($\varepsilon_r$), the substrate thickness ($l$), and the copper cladding thickness ($t$) [TEdwards1981, RKHoffmann1987, MKirschning1982]. Nonetheless, the equations are analytical, and computation of the needed width from the desired impedance is quick and simple.

**Layout Design**

The previous PCB layout used the design shown in Figure 3.7A. The main drawbacks of this layout were (1) its large area, and (2) the fact that connectors were located on both sides of the board. The large area simply meant that fewer boards could be made from a single 12“x18” piece of substrate. The fact of having connectors on both sides was more of an issue: a 270-degree electrical length connection for our design at 297.2MHz yields only a 408mm cable to connect one board to another. Layout (3.7A) requires that this cable sometimes jump from one side of one board to the other side of another. This makes putting the whole decoupling matrix together a difficult task.

Layout (3.7B) fixes this problem by putting all board/cable connectors on the same side of the board. With this design, it is possible to have all hybrid coupler boards oriented the same way, since then any 270-degree cable will only have to be bent in a semicircle to connect to any two boards. In fact, the problem of connecting all parts of the decoupling matrix was made significantly easier using layout (3.7B).

A general consideration of board layout is to minimize undesired coupling between traces. I addressed this problem by ensuring there would always be 10mm between any two traces. This was an extreme design choice, since it required large amounts of board space. However, as this prototype was a proof-of-concept, I had no problem trading this off to ensure proper performance.

Another consideration in microstrip design is to minimize impedance mismatches due to sharp bends or turns in a transmission line. Both layouts shown have many right-angled, unmitred bends, though layout (B) has fewer than layout (A). However, the effects of bends are minimal under 300MHz – even at 800MHz, the reflection at an unmitred, 90-degree bend is -40dB. Unmitred bends were chosen in this case over mitred bends because calculation of electrical length is simpler when using an unmitred bend [HJVisser2007].

**Board/Cable Connections**

Connections between board and cables were implement by using right-angle PCB/BNC connectors. From this connector, a 50Ω transmission line linked the signal path to the ring itself.

**EAGLE File Automation**
The construction of a 4-channel decoupling matrix requires up to 12 such microstrip printed circuit boards, each of differs from the others by just one design parameter: the Givens rotation angle. However, varying the impedance of a microstrip transmission line requires varying its width, which in turn affects the effective permittivity, the propagation velocity, and the electrical wavelength. Since all electrical paths need to be precisely one quarter wavelength, creating a new hybrid coupler board requires changing both the widths and lengths of all wires on the board, as well as the locations of the BNC connectors.

To simplify and streamline this process, I created MATLAB scripts that automatically generate the full EAGLE layout in a *.brd file for any hybrid ring coupler given only the desired rotation angle.

Manufacturing Process and Limitations

Boards were manufactured from substrate in-house using a T-Tech 7000 PCB router. It was found that the minimum-width copper trace that could reliably be produced using this process was 10mil (0.25mm). This corresponded to a maximum trace impedance of 160Ω and a minimum Givens rotation angle of 18 degrees.

In order to generate a Givens rotation smaller than 18 degrees, it was necessary to perform two separate rotations. Supposing we wish to rotation apply a rotation of angle \(\beta < 18^\circ\), we first apply a rotation of +45°, and second apply a rotation of \((\beta - 45)^\circ\). The net rotation will be one of angle \(\beta\), but we will have
avoided the need for impossibly thin copper traces.

Rather than use two separate boards for implement a single rotation in this case, I created an additional layout for a single board that has two integrated hybrid ring couplers, shown in Figure 3.8. The inputs of the second are connected directly to the output of the first via 50Ω transmission lines of 90° electrical length. By appropriately choosing how to connect the inputs and outputs, this design can implement an arbitrarily small Givens rotation.

In this case, the convoluted topology of the required copper trace made using right-angle PCB/BNC connectors an impossibility. Instead, I used flush PCB/BNC connectors. Unfortunately, the two types of connectors do not have the same electrical length. As such, I needed to adjust the length of the ring-to-connector 50Ω traces in order for the board-to-board connections to remain 270° when using the same cables.

**Building the Cable Interconnects**

As described in the Theory section, interconnections of precise lengths are required for the physical implementation of the decoupling matrix. In this implementation, both 270° and 450° lengths were needed. The 450° lengths include both the 270° of phase for the hybrid coupler itself, and an additional 180° of phase to perform an inversion on one input, as described previously.

The cables were manufactured out of double-shielded 50Ω coaxial cable using crimped coaxial-to-BNC connectors at both ends.

In order to verify that all cables were within one degree of electrical length of 270°, I used an automatically-calibrated test bench. The relevant electrical length that needs to be 270° is not just the length of the cable, but the total electrical distance from one physical ring to another. An illustration of this is shown in Figure 3.9. The total electrical length of the 14mm 50Ω transmission lines, the PCB/BNC connectors, and the cable needs to be this precise length. However, I did not know the exact electrical length of the connectors.

The network analyzer calibrates its transmission parameter phase measurements such that the electrical length of a standard female-to-female BNC connector, plus the fixed measurement cables, has zero degrees of phase. The measured phase of any network parameter will only be the phase difference relative to this “calibration” network. I used the same measurement cable for the duration of this experiment, so the only unknown parameter in my phase measurements was the electrical length of the f-f BNC connector.

In order to account for this fixed phase offset, while also including the phase due to the 50Ω traces and PCB/BNC connectors, I created my own auto-phase-calibration board. This board consisted of a 28mm 50Ω trace terminated by a right-angle PCB/BNC connector at each end. The 28mm trace was precisely the length of the two 14mm traces in each 270° connection, and the 2 connectors were identical to those used on all hybrid boards. In order to make phase measurements, an interconnection cable was connected this test board on one end, and an f-f BNC connector on the other. The total electrical length
of this network was: 2x14mm 50Ω copper traces, plus 2 PCB/BNC right-angle connectors, plus one interconnect cable, plus one f-f BNC connector. This is precisely the physically correct length of the interconnection, with the addition of one f-f BNC connector. Since the length of this superfluous connector is accounted for in the phase calibration, the recorded measurement is exactly the quantity we wish to measure!

For the 2-hybrid, double-rotation boards, different connectors were used which had different electrical lengths. By building a similar test board using flush PCB/BNC connectors (as opposed to right-angle PCB/BNC connectors), I was able to accurately measure this difference in electrical length. I then accounted for the different by changing the length of the 50Ω copper traces, as described previously.

**pTx Coil Connection Cables**

Four of these 270° cables did not connect two hybrid couplers, as shown in Figure 3.9, but rather connected a hybrid coupler directly to a pTx coil element. Since these 270° paths only had one right angle PCB/BNC connector and one 14mm 50Ω trace subsumed into them, the coaxial cables used needed to be longer.

**Sizing and Building Discrete Reactive Components**

There are four stages to the decoupling matrix: (1) reactance diagonalization, (2) diagonal reactance cancellation, (3) resistance diagonalization, (4) diagonal resistance matching. Stages (1) and (3) involve the diagonalization of parts of the impedance matrix, and are entirely implemented with hybrid coupler boards and coaxial interconnection cables. Stages (2) and (4), however, were implement entirely with discrete, tuned reactive elements.

**Capacitors**

For the decoupling matrix created in this experiment, capacitor values between 5pF and 45pF were needed. To implement these capacitances, tunable capacitors were used. These spanned the necessary range of capacitances, and could be accurately tuned for good matching and cancellation.

**Inductors**

Inductor values between 7nH and 40nH were needed for impedance matching and reactance cancellation. Unfortunately, I did not have access to reliable tunable inductors, and I had to build tunable inductors by hand. I implemented these as single loops of plastic-coated AWG-22 copper wire. Using empirical relationships between wire diameter, loop diameter, and inductance, I first calculated the approximate loop size for the design inductance. Then, in order to tune the inductor for precise matching or cancellation, I squeezed the loop closed or pried it further open, which reduced or increased the loop inductance.

**Measuring Decoupling Matrix S-parameters**

**Individual Board Characterization**
In order to understand how precisely the individual Givens rotations could be implemented in microstrip, I measured the S-parameters of each individual board. Measuring these parameters allowed for characterization of the actual Givens rotation angle that each board implemented.

I obtained these S-parameter measurements both with and without the necessary 270° cables. This provided crucial information about the insertion loss of the decoupling matrix. In an ideal hybrid coupler board, all power injected into port \( P_1 \) would be delivered to ports \( P_3 \) and \( P_4 \). Mathematically, this implies that: \( |S_{31}|^2 + |S_{41}|^2 = 1 \). In reality, this naturally is not the case – there is some loss associated with each hybrid board: the insertion loss. By measuring the S-parameters and calculating the quantity: \( |S_{31}|^2 + |S_{41}|^2 \), it was possible to quantify this loss. The measurements that included the 270° cables provided accurate information about the insertion loss in this implementation. However, the measurements taken directly at the connectors on the PCB – without the 270° cables – provided information on how much of that loss was due to the cables themselves. Since, as proposed, the decoupling matrix would be fully-integrated on a single PCB, this measurement is more meaningful as an assessment of the potential performance of the design.

**Decoupling Matrix Performance Characterization**

I also assessed the performance of the decoupling matrix as a whole by measuring the S-parameters of the 4-port network. I recorded these measurements at several stages during construction: (1) with only reactance diagonalization, (2) with reactance diagonalization and reactance cancellation, (3) with reactance diagonalization/cancellation, and resistance diagonalization, and (4) with reactance diagonalization/cancellation, and resistance diagonalization/matching. Measurements at each stage provided information about the performance of different parts of the decoupling matrix. Additionally, measurements of the performance of earlier stages were used to refine and update the design of the later stages. This helped later stages of the decoupling matrix partially correct for residual imperfections left over from earlier stages.

**Placement of Reactive Components**

Reactive components were inserted in series with the transmission line signal paths. In order to physically attach a series reactive element, a small (2mm) section of the copper trace was removed. The reactive element was then soldered across the newly created gap in the transmission line.
Part 4: Results

S-parameters of pTx Coil Array

In order to design the decoupling matrix, it is necessary to measure the S-parameter of the coil we plan to decouple. These s-parameters are shown in Figure 3.11. Crucially, we note that all off-diagonal S-parameters are greater than $-12dB$, including the next-nearest-neighbor $S_{13}$ and $S_{24}$ parameters. This means that there is significant coupling between coil elements in this pTx array, and that it is not removable using existing coil decoupling techniques.

Construction of Decoupling Matrix

It was found that only 9 out of a maximum of 12 Givens rotations were needed to obtain below $-26dB$ coupling between any two channels when using the 1600mL loading phantom. Thus, 9 boards were built. However, two of these needed to be small rotations, and these two boards were double-hybrid boards.

The fully-constructed decoupling matrix is shown in Figure 3.10A, and a single-hybrid board is shown in Figure 3.10B.

Measurements of Individual Boards

Measurements of Implemented Givens Rotation Angle

Givens rotation angle was measured for each individual board, whether single-hybrid or double-hybrid. The measurements are summarized in Table 3.1. All implemented Givens rotation angles were accurate to their design values to within one degree. This accuracy was observed even in boards that implemented two separate Givens rotations.

Figure 3.10: (A) Complete decoupling matrix, with all hybrid boards and cable interconnects shown. (B) close-up of individual single-hybrid board.
Table 3.1: Givens rotation angles for individual boards: design values and measured performance

<table>
<thead>
<tr>
<th>Single/Double Hybrid</th>
<th>Designed Angle</th>
<th>Measured Angle</th>
<th>Angle Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactance1 Single</td>
<td>34.5°</td>
<td>35.3°</td>
<td>+0.8°</td>
</tr>
<tr>
<td>Reactance2 Single</td>
<td>29.9°</td>
<td>29.65°</td>
<td>−0.25°</td>
</tr>
<tr>
<td>Reactance3 Single</td>
<td>28.5°</td>
<td>28.0°</td>
<td>+0.5°</td>
</tr>
<tr>
<td>Reactance4 Single</td>
<td>23.5°</td>
<td>23.5°</td>
<td>0.0°</td>
</tr>
<tr>
<td>Reactance5 Single</td>
<td>23.8°</td>
<td>22.9°</td>
<td>−0.9°</td>
</tr>
<tr>
<td>Resistance4 Single</td>
<td>26.1°</td>
<td>26.0°</td>
<td>−0.1°</td>
</tr>
<tr>
<td>Resistance5 Double</td>
<td>17.8°</td>
<td>17.9°</td>
<td>+0.1°</td>
</tr>
<tr>
<td>Resistance6 Single</td>
<td>36.2°</td>
<td>36.7°</td>
<td>+0.5°</td>
</tr>
<tr>
<td>Resistance1 Double</td>
<td>2.85°</td>
<td>3.49°</td>
<td>+0.54°</td>
</tr>
</tbody>
</table>

Table 3.2: Insertion losses for individual boards: design values and measured performance

<table>
<thead>
<tr>
<th>Single/Double Hybrid</th>
<th>Loss (w/Cables)</th>
<th>Loss (no Cables)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactance1 Single</td>
<td>−0.33dB</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Reactance2 Single</td>
<td>−0.26dB</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Reactance3 Single</td>
<td>−0.26dB</td>
<td>−0.057dB</td>
<td>−0.203dB</td>
</tr>
<tr>
<td>Reactance4 Single</td>
<td>−0.28dB</td>
<td>−0.072dB</td>
<td>−0.208dB</td>
</tr>
<tr>
<td>Reactance5 Single</td>
<td>−0.27dB</td>
<td>−0.069dB</td>
<td>−0.201dB</td>
</tr>
<tr>
<td>Resistance4 Single</td>
<td>−0.26dB</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Resistance5 Double</td>
<td>−0.405dB</td>
<td>−0.110dB</td>
<td>−0.295dB</td>
</tr>
<tr>
<td>Resistance6 Single</td>
<td>−0.255dB</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Resistance1 Double</td>
<td>−0.395dB</td>
<td>−0.084dB</td>
<td>−0.311dB</td>
</tr>
</tbody>
</table>
Measurements of Insertion Loss

Insertion loss was measured for each individual board, with and without interconnection cables. The results are summarized in Table 3.2. All single-hybrid board insertion losses measured between $-0.26dB$ and $-0.33dB$ with cables, and between $-0.057dB$ and $-0.072dB$ without them. For double-hybrid boards, the corresponding insertion loss ranges were $-0.395dB$ to $-0.405dB$ and $-0.084dB$ to $-0.110dB$. Several “no-cable” measurements are missing. For these boards, the network analyzer did not give physically possible results – it reported positive decibel values. Since these boards are passive networks, this is not possible and the measurements are not reported here.

Measurements of System Performance

The entire decoupling matrix consists of several blocks, as illustrated in Figure 3.12. Building the decoupling matrix involved building and connecting each of these blocks – (1) the reactance diagonalization block, (2) the diagonal reactance cancellation block, (3) the resistance diagonalization block, and (4) the single-port resistance matching block – to the pTx coil in the proper order. To assess

![Diagram](image.png)

Figure 3.12: The pTx decoupling matrix comprises a reactance diagonalization block, a reactance cancellation block, a resistance diagonalization block, and a single-port resistance matching block. These blocks are connected to the pTx coil array in that order. In order to observe the performance of each block, S-parameters when looking into each section of the decoupling matrix were measured (Meas. 1-4).
the performance of each block, the S-parameters of the system were measured after each new block was attached. This is equivalent to obtaining S-parameter measurements looking into the system at the arrows labeled “Meas. 1” through “Meas. 4” in Figure 3.12. Figures 3.13 through 3.16 show the measurements obtained at each point in the system.
Figure 3.13 - Meas 1: (A) Measured reactance parameters looking into the reactance diagonalization block. (B) plot of measured reactance parameters vs. frequency

Figure 3.14 - Meas 2: (A) Measured reactance parameters looking into the reactance cancellation block. (B) plot of measured reactance parameters vs. frequency

### Meas. 1

<table>
<thead>
<tr>
<th></th>
<th>$X_{11}$</th>
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<th>$X_{13}$</th>
<th>$X_{14}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16.2Ω</td>
<td>-2.7Ω</td>
<td>-0.2Ω</td>
<td>-0.2Ω</td>
</tr>
<tr>
<td>2</td>
<td>2.5Ω</td>
<td>-19.4Ω</td>
<td>3.7Ω</td>
<td>-0.5Ω</td>
</tr>
<tr>
<td>3</td>
<td>2.0Ω</td>
<td>3.7Ω</td>
<td>-15.0Ω</td>
<td>1.5Ω</td>
</tr>
<tr>
<td>4</td>
<td>0.2Ω</td>
<td>-0.4Ω</td>
<td>1.4Ω</td>
<td>-15.9Ω</td>
</tr>
</tbody>
</table>

### Meas. 2

<table>
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<th>$X_{14}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.8Ω</td>
<td>-1.9Ω</td>
<td>-0.2Ω</td>
<td>-0.1Ω</td>
</tr>
<tr>
<td>2</td>
<td>-2.0Ω</td>
<td>-0.3Ω</td>
<td>-0.6Ω</td>
<td>-3.1Ω</td>
</tr>
<tr>
<td>3</td>
<td>-0.3Ω</td>
<td>-0.6Ω</td>
<td>-1.3Ω</td>
<td>-0.7Ω</td>
</tr>
<tr>
<td>4</td>
<td>0.0Ω</td>
<td>-2.9Ω</td>
<td>-0.7Ω</td>
<td>-0.6Ω</td>
</tr>
</tbody>
</table>
Figure 3.15 - Meas 3: (A) Measured resistance parameters looking into the resistance diagonalization block. (B) plot of measured resistance parameters vs. frequency. (C) Measured reactance parameters looking the resistance diagonalization block. (D) plot of measured reactance parameters vs. frequency

### Meas. 3 A

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<tr>
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<tbody>
<tr>
<td>6.2 $\Omega$</td>
<td>-0.8 $\Omega$</td>
<td>0.6 $\Omega$</td>
<td>0.2 $\Omega$</td>
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<table>
<thead>
<tr>
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<th>$R_{22}$</th>
<th>$R_{23}$</th>
<th>$R_{24}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.8 $\Omega$</td>
<td>24.1 $\Omega$</td>
<td>0.0 $\Omega$</td>
<td>-1.0 $\Omega$</td>
</tr>
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</table>

<table>
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<th>$R_{32}$</th>
<th>$R_{33}$</th>
<th>$R_{34}$</th>
</tr>
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<tbody>
<tr>
<td>0.6 $\Omega$</td>
<td>0.0 $\Omega$</td>
<td>39.4 $\Omega$</td>
<td>-0.3 $\Omega$</td>
</tr>
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<table>
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<th>$R_{42}$</th>
<th>$R_{43}$</th>
<th>$R_{44}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2 $\Omega$</td>
<td>-1.0 $\Omega$</td>
<td>-0.3 $\Omega$</td>
<td>33.6 $\Omega$</td>
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</table>

### Meas. 3 C

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<th>$X_{14}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>-15.0 $\Omega$</td>
<td>0.9 $\Omega$</td>
<td>1.2 $\Omega$</td>
<td>-0.9 $\Omega$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
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<th>$X_{22}$</th>
<th>$X_{23}$</th>
<th>$X_{24}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9 $\Omega$</td>
<td>-45.6 $\Omega$</td>
<td>-1.4 $\Omega$</td>
<td>1.0 $\Omega$</td>
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</table>

<table>
<thead>
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<th>$X_{32}$</th>
<th>$X_{33}$</th>
<th>$X_{34}$</th>
</tr>
</thead>
<tbody>
<tr>
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<td>-1.4 $\Omega$</td>
<td>0.7 $\Omega$</td>
<td>0.3 $\Omega$</td>
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<table>
<thead>
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<th>$X_{42}$</th>
<th>$X_{43}$</th>
<th>$X_{44}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>-0.9 $\Omega$</td>
<td>1.0 $\Omega$</td>
<td>0.3 $\Omega$</td>
<td>-8.0 $\Omega$</td>
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</table>
Figure 3.16: (A) Measured Coil S-parameters. (B) plot of measured coil S-parameters vs frequency. (C) Measured S-parameters of entire decoupling matrix, looking into impedance matching block. (D) Plot of decoupling matrix S-parameters vs frequency.

Meas. 4

<table>
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</thead>
<tbody>
<tr>
<td>$-8,\text{dB}$</td>
<td>$-11,\text{dB}$</td>
<td>$-10,\text{dB}$</td>
<td>$-11,\text{dB}$</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>$S_{21}$</th>
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<th>$S_{23}$</th>
<th>$S_{24}$</th>
</tr>
</thead>
<tbody>
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<td>$-11,\text{dB}$</td>
<td>$-6,\text{dB}$</td>
<td>$-12,\text{dB}$</td>
<td>$-11,\text{dB}$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$S_{31}$</th>
<th>$S_{32}$</th>
<th>$S_{33}$</th>
<th>$S_{34}$</th>
</tr>
</thead>
<tbody>
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<td>$-10,\text{dB}$</td>
<td>$-12,\text{dB}$</td>
<td>$-5,\text{dB}$</td>
<td>$-12,\text{dB}$</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>$S_{41}$</th>
<th>$S_{42}$</th>
<th>$S_{43}$</th>
<th>$S_{44}$</th>
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<tr>
<td>$-11,\text{dB}$</td>
<td>$-12,\text{dB}$</td>
<td>$-6,\text{dB}$</td>
<td>$6,\text{dB}$</td>
</tr>
</tbody>
</table>

B

D

$S_{ij}$

$S_{ii}$
Reactance Diagonalization Performance (Figure 3.13 - Meas 1)

The performance of the reactance diagonalization block was measured by analyzing the Z-parameters looking into it. Specifically, we looked at the imaginary parts of the off-diagonal Z-matrix terms, as these are the off-diagonal reactances that we hope to remove. As shown in Figure 3.13, all these off-diagonal reactance terms were reduced below $4\Omega$ in magnitude.

Reactance Cancellation Performance (Figure 3.14 - Meas 2)

The performance of the diagonal reactance cancellation block measured by analyzing its Z-parameters. After this stage, all reactances – both diagonal and off-diagonal – should be reduced to zero. As shown in Figure 3.14, all reactances were in fact reduced below $3.1\Omega$ in magnitude after this stage.

Resistance Diagonalization Performance (Figure 3.15 - Meas 3)

After the resistance diagonalization block, we hoped to see the real (resistive) part of all off-diagonal Z-parameters reduced to zero. As shown in Figure 3.15A, this is nearly the case. All off-diagonal resistances were below $1\Omega$ in magnitude.

We also hoped to preserve the effects of the previous reactance removal stages and observe zero reactance for diagonal and off-diagonal Z-parameters. However, because of a probable measurement error, there was residual reactance in the Z-matrix at this stage. It was, however, successfully diagonalized, as shown in Figure 3.15C, so that it could still be cancelled by the single-port matching stage. This issue is explored in the Discussion section.

Resistance Matching Performance (Figure 3.16 - Meas 4)

After inserting single-port matching networks, we expected the system to be fully-matched to the independent, $50\Omega$ RF power amplifiers. This condition is met when all S-parameters looking into the decoupling matrix are equal to zero. As shown in Figure 3.16C, this is nearly the case: after applying the single-port matching networks, all S-parameters were reduced below $-26dB$. Compared to the initial coupling levels of over $-12dB$ (Figure Meas 4 (A)), this is a significant improvement. Overall, reduction in coupling between any two channels to only $-26dB$ is a significant accomplishment, and proves the potential for using decoupling matrices to improve pTx coil performance.

Decoupling Matrix Performance Under Load Variations

We measured the performance of the decoupling matrix when the pTx coil was loaded with different-sized phantoms, as described in the Methods section. For this part, we only measured the S-parameters of the whole system, and did not observe the performance at each stage.

The measured S-parameters at different loading conditions are plotted against frequency in Figure 3.17. For phantom (i), all S-parameters were under $-26dB$. For phantom (ii), they were all below $-22dB$. For phantom (iii), they were all below $-18dB$. In the case of phantom (iii), the only S-parameters above $-20dB$ were the two diagonal S-parameters $S_{22}$ and $S_{33}$. 
Figure 3.17: (a) Pictures of the 1600mL phantom (i), 2000mL phantom (ii), and 2700mL phantom (iii) used to load the pTx coil. (b) S-Params of decoupling matrix under phantom (i) loading. (c) S-Params of decoupling matrix under phantom (ii) loading. (d) S-Params of decoupling matrix under phantom (iii) loading.
Part 5: Discussion

Decoupling Matrix Performs as Designed

Individual Hybrid Performance

The printed circuit boards that implemented Givens rotations all matched their design rotation angle to within one degree. This was a good match: in ADS simulations, such a variation in the actual rotation angle of any hybrid coupler did not affect the performance of the system. Additionally, this information on microstrip precision is valuable for designing the decoupling matrix to account for process variations.

Decoupling Performance

The decoupling matrix successfully reduced all S-parameters of the pTx coil array to below $-26dB$. Since the fully-coupled pTx coil array had all coupling S-parameters between $-12dB$ and $-10dB$, this implies that the decoupling matrix has resulted in a significant improvement. Additionally, all next-nearest-neighbor S-parameters have been reduced below $-26dB$ when using the decoupling matrix. This type of performance is not possible with other decoupling strategies, and illustrates an advantage of the decoupling matrix strategy over others.

Load Sensitivity

It was observed that the decoupling matrix successfully decoupled the pTx channels under different coil loading conditions. The design goal of reducing all S-parameters below $-20dB$ was met under all conditions, excepting two reflection S-parameters when loaded with the largest phantom. In this case, all coupling S-parameters were below $-20dB$, suggesting that the impedance matrix diagonalization stages still performed as designed. Only $S_{22}$ and $S_{33}$ did not meet specifications, implying that the single-port matching networks used on those ports were not robust enough to changing load conditions.

In our implementation, we used L-match networks as the single-port matching networks for the Diagonal Resistance Matching stage. The L-match topology, however, results in an impedance match with a very high Q-factor, meaning that the impedances are only well-matched over a very narrow bandwidth for a given load. We suspect that, when a different loading phantom was used and this load changed, the resulting bandwidth was too narrow, and did not include 297.2 MHz – the frequency of interest.

To fix this, we could use a different single-port matching network with a lower Q-factor. Examples of such networks are Pi- and T-match networks. The increased bandwidth resulting from these networks would be expected to reduce the sensitivity of the reflection parameters $S_{ii}$ to load variations.

Measured Insertion Loss Is Low Enough for Decoupling Matrices to Be Viable

It is important to remember the main reason for wanting to reduce coupling between elements of a pTx coil: reducing coupling improves power delivery to the load and requires less power to be generated by
the RF power amplifiers. Thus, the decoupling matrix will only be worthwhile if the introduced insertion loss is lower than the improvement in power delivery to the load.

This is indeed what we observed. Without the decoupling matrix, the fully-coupled pTx coil had off-diagonal S-parameters of approximately $-11\,dB$, and diagonal S-parameters of approximately $-7\,dB$. This means that roughly 20% of power injected on one port was reflected back to that same port. Of the 80% that was delivered to the pTx coil, about 10% was reflected back on each of the three other ports. Thus, 30% of injected power was reflected back on the other ports – an effective loss of $-1.5\,dB$.

With the decoupling matrix, all off-diagonal terms were under $-26\,dB$, implying under 0.25% of injected power is reflected back on one of the other ports. Multiplying this by three ports, this is an effective loss of $-0.033\,dB$.

We also need to consider the additional insertion loss from all the hybrid couplers required to implement a decoupling matrix. In our implementation, there is significant loss due to the many cables and connectors used in the construction of the matrix. Using an insertion loss of $-0.3\,dB$ for a single board+cables, and assuming a full 6 series boards are needed for each channel, we find an insertion loss of $-1.8\,dB$. This is greater than the loss due to coupling, suggesting that a full implementation as we have built it will not result in reduced power consumption.

However, a future implementation would not use discrete boards for each Givens rotations, and would not require so many cables and manually-soldered connections. The proposed architecture would be similar previous work in fully-integrated, microstrip Butler matrices for 7T MRI [PYazdanbakhsh2011]. As seen in the insertion loss measurements for hybrid coupler boards with and without the cables, the majority of the insertion loss is due to these cables+connectors, and not due to the PCBs themselves. In fact, the average measured insertion loss for a single-hybrid board without cables was $-0.07\,dB$. Using this figure, we find an expected total insertion loss of $-0.42\,dB$ for a 4-channel pTx coil. This is a significant improvement over the $-1.5\,dB$ of observed loss due to channel coupling.

Furthermore, there is reason to believe the insertion loss may be even lower with a fully-integrated implementation. For single-hybrid boards, the insertion loss was $-0.07\,dB$ when measured without the cables. However, this included both the loss due to the microstrip path and the loss due to the PCB/BNC connectors. A fully-integrated version would not include a pair of connectors for each hybrid – the hybrid couplers would be connected to each other directly by microstrip interconnects. We can get an idea of the expected insertion loss in this base by comparing the single-hybrid board insertion loss to the double-hybrid board insertion loss. For double-hybrid boards, the measured insertion loss was, on average $-0.10\,dB$ excluding cables. Comparing this to the insertion loss of a single-hybrid board, we find that the additional insertion loss introduced by adding only a microstrip hybrid coupler, plus microstrip interconnections, was $-0.03\,dB$. This measurement represents only the loss from a microstrip hybrid coupler, as it includes no additional connectors or cables. If we use this value to estimate the insertion loss of a fully-integrated 4-channel decoupling matrix, we find a total loss of $-0.18\,dB$. This represents a theoretical minimum loss for this design on Rogers 3003 substrate, and would be a huge improvement in power over the fully-coupled pTx coil.
Later Stages of the Decoupling Matrix Can Compensate for Imperfect Performance of Earlier Stages

In Figure Meas 2, it was shown that all reactances were reduced below 3.1Ω in magnitude. However, in Figure Meas 3, several diagonal reactance terms were clearly much larger than this value. I believe that this discrepancy arose by failing to properly account for electrical path length in the conversion between Z-parameters and S-parameters. The result was unexpected residual phase in the Z- and S-parameters of the system, which is equivalent to having undesired reactance.

I was, however, able to account for this unwanted reactance during the Resistance Diagonalization and Diagonal Resistance Matching stages. There are two important observations behind this. (1) Single-port matching can account for any diagonal reactance, in addition to matching the diagonal resistances. It does this by introducing addition shunt or series reactance in the network – essentially, it performs another Diagonal Reactance Cancellation. (2) If the appropriate reactance elements are inserted before a Givens rotation in the Resistance Diagonalization Block, then that very Givens rotation can diagonalize both the resistive and reactive parts of the Z-matrix. Implementing both of these steps allows for residual reactance to be removed during the Resistance Diagonalization and Matching stages of the decoupling matrix.
Part 6: Conclusion

Building on previously-developed theory and design tools for decoupling matrices, I was able to construct a functional physical proof-of-concept prototype that met all design specifications. My hardware demonstration proved that decoupling matrices successfully eliminate coupling between all elements of a pTx array, that the performance is robust to changing load conditions, and that the introduced power loss can be minimal. All of these facts suggest that decoupling matrices for pTx coils have the potential to be a valuable contribution to technology development for high-field MRI.
References:


Kirschning, M; Jansen, RH. *Accurate Model for Effective Dielectric Constant with Validity up to Millimeter-Wave Frequencies*. Electronics Letters. 18:272-273 (Jan 1982).


