

DESIGN, CHARACTERIZATION AND VALIDATION OF A SINGLE-SIDED FIELD
FREE LINE SCANNER FOR MAGNETIC PARTICLE IMAGING

by

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Dedicated to
my father Gerald, and my mother Paula

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I consider myself fortunate in many ways to have been given the opportunity to pursue this PhD. It is a rare and unique experience to contribute to hardware development at such an early stage within an emerging field. Throughout this journey, I have also been fortunate to work with and learn from many talented individuals, people with deep technical knowledge and a genuine passion for science. My growth as a researcher was made possible by many people, and I would like to acknowledge some of those here.

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Christopher Paul McDonough

ABSTRACT

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Magnetic particle imaging (MPI) is an emerging tracer based imaging modality capable of detecting superparamagnetic iron oxide (SPIO) nanoparticles with high sensitivity, positive contrast, and without ionizing radiation. These properties make MPI promising for a wide range of biomedical applications, including cancer detection, cell tracking, vascular imaging, and image guided interventions. Preclinically, MPI has demonstrated strong performance, but translation to human scale imaging has remained limited by hardware constraints. Traditional closed bore MPI scanners are not scalable to full human imaging, as the magnetic field strengths required over such volumes demand infeasible power consumption. As a result, hardware development remains an active area of research in MPI, with many groups exploring alternative scanner designs targeted to specific anatomies or employing non conventional geometries.

One promising alternative is the single-sided scanner geometry. Single-sided geometries confine all hardware to one side of the imaging subject, enabling open access and accommodating anatomies that cannot be imaged using traditional closed bore designs. However, this topology also presents inherent challenges, most notably inhomogeneous magnetic fields which complicate imaging and limit penetration depth. Additionally, scanners of this topology have traditionally suffered from insufficient

sensitivity, restricting them from biological applications where microgram sensitivity is required, such as in-vivo applications.

This dissertation presents the design, development, characterization, and validation of a single-sided field free line (FFL) MPI scanner, with a future goal of translation to breast imaging applications. The system addresses challenges traditionally associated with single-sided MPI through multiple design choices, including the use of an FFL for spatial encoding, which provides increased sensitivity. Demonstrated in this work are a theoretical analysis, numerical simulation, and experimental validation of the scanner. Imaging studies using a variety of phantoms establish technical performance and demonstrate suitability for anatomical imaging. In addition, ex vivo imaging of labeled cancer cells demonstrates biologically relevant detection sensitivity, and preliminary in vivo imaging studies in mice further support the translational potential of this approach. Together, these results advance single-sided MPI as a viable imaging topology and outline a potential pathway for extending MPI toward clinical applications.

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LIST OF ABBREVIATIONS

AC	Alternating Current
CAD	Computer-Aided Design
CNN	Convolutional Neural Network
CT	Computed Tomography
DC	Direct Current
FBP	Filtered Back Projection
FDA	Food and Drug Administration
FFL	Field-Free Line
FFP	Field-Free Point
FFR	Field-Free Region
FFT	Fast Fourier Transform
FOV	Field of View
FWHM	Full Width at Half Max
MBI	Molecular Breast Imaging
ML	Machine Learning
MPI	Magnetic Particle Imaging
MPS	Magnetic Particle Spectrometer
MRI	Magnetic Resonance Imaging
MSE	Mean Squared Error
NHP	Non-Human Primate
NIH	National Institutes of Health
PBS	Phosphate Buffered Saline
PET	Positron Emission Tomography
PSF	Point Spread Function
ROI	Region of Interest
Rx	Receive (Coil)
SLNB	Sentinel Lymph Node Biopsy
SNR	Signal to Noise Ratio
SPECT	Single-Photon Emission Computed Tomography
SPIO	Superparamagnetic Iron Oxide (Nanoparticle)
Tx	Transmit (Coil)

CHAPTER ONE

INTRODUCTION

1.1 Clinical Motivation

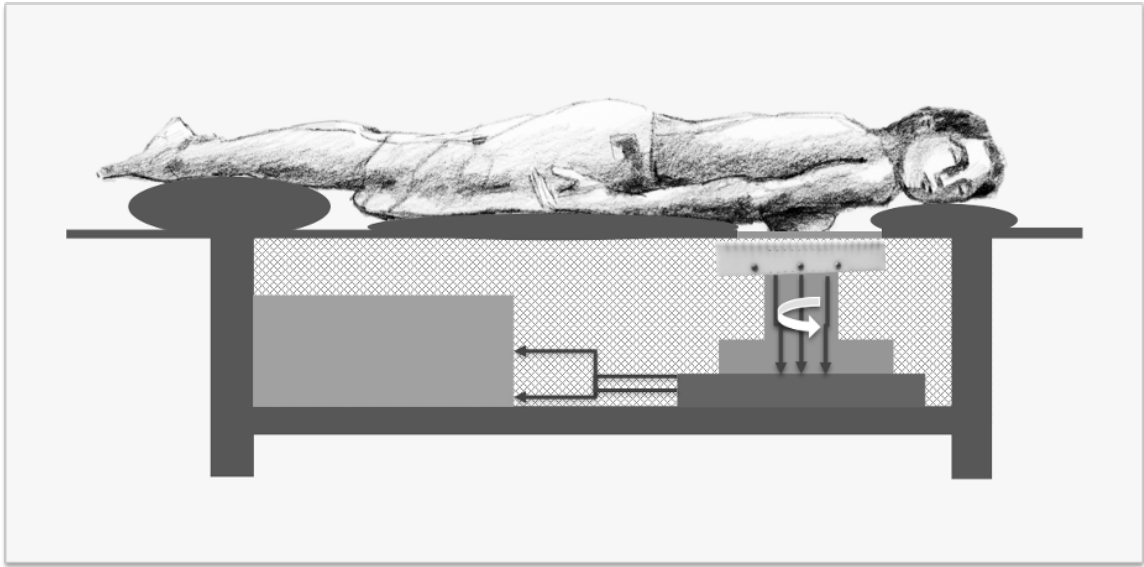


Figure 1.1: **Conceptual design for a human-scale breast magnetic particle imaging (MPI) scanner utilizing a single-sided field free line (FFL) geometry.** An integrated single-sided MPI scanner with a patient table, showing the patient comfortably lying in the prone position.

Breast cancer is the most prevalent cancer among women worldwide and in the United States [1]. The current standard screening method, x-ray mammography, has an overall sensitivity of around 80% [2]. However, its effectiveness significantly decreases for women with dense breast tissue, leading to higher rates of false positives and false negatives [3]. Additionally, mammography is associated with considerable patient

discomfort. Other imaging modalities, such as magnetic resonance imaging (MRI), ultrasound, computed tomography (CT), and single-photon emission computed tomography (SPECT) used for molecular breast imaging (MBI), are available but are generally used as supplemental techniques due to limitations in sensitivity, cost, imaging time, and the use of ionizing radiation [4]. These challenges highlight the need for a novel screening approach that is safe, highly sensitive, cost-effective, and robust (see Fig. 1.1).

In addition to early detection, precise localization of malignant cells is crucial for effective breast cancer treatment. Breast-conserving surgery remains a preferred option, but complete tumor removal is essential to prevent recurrence. Therefore, intra-operative imaging techniques to delineate tumor margins are currently under development [citmaloney2018review](#). One example of an emerging method to distinguish normal from cancerous tissue is photoacoustic imaging. This non-invasive, high contrast imaging method visualizes differences in optical absorption using a pulsed laser to elicit an acoustic response from tissue [5]. Another critical aspect of breast cancer management is assessing metastasis. Historically, axillary lymph node dissection was performed for staging [6], but it has been largely replaced by sentinel lymph node biopsy (SLNB) [7], [8], which relies on dyes and radioactive tracers. However, false-positive results and unnecessary biopsies remain a significant concern [9]. A new non-radioactive tracer, combined with a highly sensitive and safe imaging technique, could provide a transformative alternative to current standards, improving diagnostic accuracy and patient outcomes.

Magnetic particle imaging (MPI) is another emerging tracer-based biomedical imaging modality capable of detecting superparamagnetic iron oxide (SPIO) nanoparticles with exceptional sensitivity, contrast, and high spatiotemporal resolution [10]. MPI is considered a safe imaging technique, as it does not involve ionizing radiation and utilizes non-toxic SPIO tracers, some of which have been approved for use in magnetic resonance

imaging (MRI) applications [11], [12]. Similarly to MBI, MPI has the potential to use specific biomarkers to distinguish between malignant and benign tumors by conjugating SPIO with a chemical agent [13]. Therefore, the MPI technique could provide a transformative alternative to current standards in both diagnostic imaging and tumor margin detection, improving diagnostic accuracy and patient outcomes.

1.2 MPI Overview

Magnetic particle imaging (MPI) is a promising tracer-based imaging modality which detects super paramagnetic iron oxide nanoparticles (SPIOs). The theory behind MPI was first conceived of by two physicists in 2001: Bernhard Gleich and Jürgen Weizenecker at the Philips Research Laboratory in Germany. In January 2005, Gleich and Weizenecker published the first MPI images in the scientific journal Nature [10], starting the field. Although the field is still in the preclinical stage, MPI shows great promise and will likely be the first new imaging modality to come to medicine in three decades.

MPI features many promising aspects, such as its safety due to not utilizing ionizing radiation. The lack of ionizing radiation makes MPI very desirable due to the belief that up to 2% of future cancers could be induced by radiation from medical imaging [14]. Even MRI, an imaging modality which also doesn't use ionizing radiation, frequently requires contrast agents (i.e. gadolinium) for certain clinical applications, including brain, spine, and vascular imaging, particularly when evaluating tumors, inflammation, or infection. Gadolinium has been shown to accumulate in the brain, bones, and other organs and may have long term effects [15]. The SPIOs used in MPI, on the other hand, are commonly considered to be safe for clinical use. In fact, Ferumoxytol, a drug containing SPIO is already approved for intravenous use by the FDA for treatment of anemia [11], [12], [16].

In addition to safety, MPI has other advantages over other modalities including high temporal resolution and high sensitivity. MPI is also an ideal tracer based imaging

modality, meaning no background signal from the human body is measured. Additionally various groups have shown the viability of MPI for the following biomedical applications cell tracking [17], [18], cancer imaging [19], and hyperthermia [20]–[22].

Over the past decade, MPI technology has advanced rapidly, leading to the development of commercial preclinical MPI systems with small-bore designs, such as those offered by Bruker (Karlsruhe, Germany) and Magnetic Insight (Alameda, CA). The utility of MPI imaging was demonstrated in a variety of preclinical applications such as angiography [23], [24] and perfusion [25]; cancer imaging [26], cell tracking [17], [27], hyperthermia [28], [29], and real-time tracking of interventional instruments: e.g., balloon catheters in cardiovascular procedures [30], [31]. Significant research efforts are underway globally to develop human-sized MPI systems, with a primary focus on closed-bore, head-only scanners [32]–[35] and targeted applications in functional MPI [36] and cancer detection and treatment [37]. Recently utility for interventional procedures was demonstrated with the leg interventional scanner, iMPI [38], [39]. Despite these advancements, the extension of MPI technology to whole-body imaging remains challenging due to safety concerns and the high power requirements associated with closed-bore geometries [40].

One notable design is the single sided scanner which was first proposed by Sattel et al. in 2009 [41]. The single sided scanner confines all hardware to a single side of the device, which is beneficial because it provides the patient with unrestricted access to the scanning area [42]. The downside to the single sided scanner is that imaging is made more difficult, and the scanner must necessarily have a limited penetration depth [43]. We aim to improve upon the original single sided scanner [41], which utilizes a field free point (FFP), by utilizing a field free line (FFL) instead [44], [45]. Utilizing a FFL promises a higher sensitivity [46] and more robust image reconstruction [47].

1.3 Physics of MPI

The goal of this section is to briefly describe the physics and theory that govern MPI, a more detailed discussion is provided in Chapter 2. At its core, MPI measures a quantitative signal generated by magnetic tracer particles and spatially encodes that signal to produce an image of their distribution within a region of interest. Signal generation is typically achieved by applying an alternating magnetic field to the SPIO sample using an electromagnetic coil, referred to interchangeably in this work as an excitation coil or a drive coil. This field induces an oscillating magnetization in the particles, which is measured as a voltage in a receive coil due to Faraday induction. Spatial encoding is accomplished by applying a magnetic field gradient, generated using either permanent magnets or electromagnets, which localizes the region of signal generation and thus allow for imaging.

Although alternative approaches have been proposed for both signal generation and spatial encoding, the techniques described here are the most widely used and are employed in the system presented in this work. The remainder of this section explains the theory of these methods in greater detail.

1.3.1 SPIO Magnetic Properties

As a tracer-based imaging modality, MPI relies fundamentally on the magnetic properties of its tracer particles. The suitability of a particle for MPI is determined by how strongly it responds to an applied magnetic field, which in turn determines performance metrics such as spatial resolution and sensitivity. The tracers used in MPI are typically superparamagnetic iron oxide nanoparticles (SPIOs), chosen for their strong nonlinear magnetization response and biocompatibility.

Superparamagnetism is a magnetic phenomenon observed in small ferromagnetic or ferrimagnetic nanoparticles (< 100 nm), where the small size causes the particle to consist of a single magnetic domain. Unlike ferromagnets, superparamagnetic materials

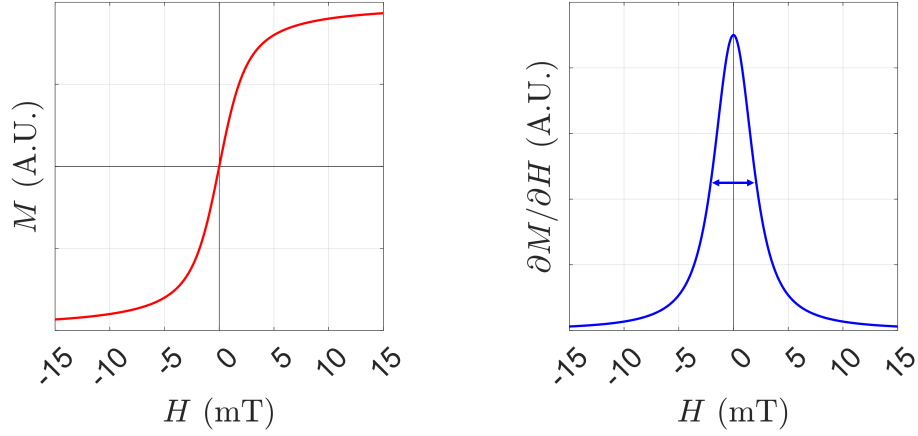


Figure 1.2: **Langevin magnetization and its derivative.** Magnetization $M(H)$ of a superparamagnetic nanoparticle ensemble described by the Langevin function, illustrating nonlinear dependence on applied magnetic field H . Corresponding field derivative $\partial M/\partial H$, which defines the spatial resolution and sensitivity of MPI.

exhibit no remanent magnetization in the absence of an external field, a desirable property for MPI. When an external magnetic field is applied, the individual magnetic particle moments $\vec{m}$ align with the field, producing a macroscopic magnetization $\vec{M}$, achieving saturation at low field values (~ 10 mT). The magnitude and nonlinearity of this response are what enable SPIOs to act as effective tracers in MPI.

A basic model for the magnetization behavior of SPIOs is provided by Langevin theory¹, which assumes the particles are in thermal equilibrium. According to this model, the net magnetization $\vec{M}$ of the tracer ensemble in response to an applied magnetic field $\vec{H}$ is given by:

$$\vec{M}(\vec{H}) = cm\mathcal{L}(\beta|\vec{H}|)\hat{H} \quad (1.1)$$

Here, c is the particle concentration, m is the magnetic moment of an individual particle, and $\mathcal{L}()$ is the Langevin function. The parameter β quantifies the ratio of magnetic to

¹A full derivation of Langevin theory of paramagnetism is provided in Appendix A.1.

thermal energy and is given by

$$\beta = \frac{\mu_0 m}{k_B T} \quad (1.2)$$

where μ_0 is the vacuum permeability, k_B is Boltzmann's constant, and T is the absolute temperature.

The Langevin function is defined as

$$\mathcal{L}(\xi) = \begin{cases} \coth(\xi) - \frac{1}{\xi}, & \xi \neq 0, \\ 0, & \xi = 0. \end{cases} \quad (1.3)$$

The derivative of the Langevin function is thus

$$\mathcal{L}'(\xi) = \begin{cases} \frac{1}{\xi^2} - \frac{1}{\sinh^2(\xi)}, & \xi \neq 0, \\ \frac{1}{3}, & \xi = 0. \end{cases} \quad (1.4)$$

Figure 1.2 illustrates the Langevin magnetization curve of a SPIO ensemble and its corresponding field derivative. Note the nonlinear dependence² of the magnetization on the applied magnetic field, this nonlinearity is critical for separating the useful signal originating from the SPIO tracer from the large background present in MPI. Also shown is the field derivative $\partial M / \partial H$, which exhibits a bell-shaped profile with a peak centered at $H = 0$. The peak amplitude of this curve determines the strength of the detected MPI signal, since the MPI signal is proportional to $\partial M / \partial H$. In addition, the full width at half maximum (FWHM) of $\partial M / \partial H$ determines the achievable spatial resolution, with a sharper peak corresponding to superior resolution. This arises because magnetic gradient fields are used to spatially localize the signal response in MPI. A more detailed

²Linear dependence of classical paramagnetism can be derived from the low-field ($\beta|\vec{H}| \ll 1$) approximation of superparamagnetism and is shown in Appendix A.2.

explanation of how SPIO properties inform the signal and spatial resolution is provided in the following sections.

1.3.2 Signal Detection and Sensitivity

For signal detection in MPI an oscillating magnetic field $\vec{H}(t)$ is applied to the SPIO sample, inducing an oscillating magnetization $\vec{M}(t)$ in that sample. The resulting oscillating magnetization creates a changing magnetic field which can be detected in a receive coil due to Faraday's law of induction. Faraday's law of induction states that a changing magnetic flux through the cross section of coil induces a voltage $u(t)$ in that coil. This voltage is given by:

$$u(t) = -\mu_0 \frac{d}{dt} \oint_S \vec{H}(x, y, z, t) \cdot d\vec{S} \quad (1.5)$$

where $\vec{H}(x, y, z, t)$ is the total magnetic field inside of the coil, and S is the surface area of the coil. Using the law of reciprocity³ Faraday's law of induction instead becomes an integration over the volume where the particles are located. This more illuminating form of Faraday's law of induction takes on the form:

$$\begin{aligned} u(t) &= -\frac{d}{dt} \int_{\text{particles}} \vec{P}^R(x, y, z) \cdot \vec{M}(x, y, z, t) dV \\ &= -\int_{\text{particles}} \vec{P}^R(x, y, z) \cdot \frac{\partial \vec{M}(x, y, z, t)}{\partial t} dV \end{aligned} \quad (1.6)$$

where $\vec{P}^R(x, y, z)$ is the sensitivity profile of the receive coil and is the same as the magnetic field when there is unit current in the coil ($\vec{P}_{\text{coil}} = \vec{B}_{\text{coil}}(I_{\text{coil}} = 1 \text{ A})$). To clarify the dependence of the detected signal $u(t)$ on the magnetic properties of the SPIO tracer, Eq. 1.6 can be rewritten using the chain rule as

$$u(t) = -\int_{\text{particles}} \vec{P}^R(x, y, z) \cdot \left(\frac{\partial \vec{M}}{\partial \vec{H}} \cdot \frac{\partial \vec{H}(x, y, z, t)}{\partial t} \right) dV. \quad (1.7)$$

³A derivation of the law of reciprocity as applied to MPI signal detection is provided in Appendix A.3.

In general, the quantity $\partial \vec{M} / \partial \vec{H}$ is a second-order tensor describing the differential magnetic susceptibility of the tracer. However, for superparamagnetic particles described by the Langevin model the magnetization is parallel to the applied magnetic field. Under this condition the tensor reduces to a scalar derivative along the field direction and

$$\frac{\partial \vec{M}}{\partial t} = \frac{\partial M}{\partial H} \frac{\partial \vec{H}}{\partial t}. \quad (1.8)$$

Substituting this relation into Eq. 1.7 yields the commonly used MPI signal equation

$$u(t) = - \int_{\text{particles}} \vec{P}^R(x, y, z) \cdot \left(\frac{\partial M}{\partial H} \frac{\partial \vec{H}(x, y, z, t)}{\partial t} \right) dV. \quad (1.9)$$

This expression shows that the detected MPI signal is proportional to the field derivative of the tracer magnetization, $\partial M / \partial H$, as well as to the rate of change of the applied magnetic field $\partial H / \partial t$. Consequently, tracers exhibiting a larger magnetic susceptibility (χ) generate stronger induced voltages in the receive coil, thereby improving signal magnitude and achievable sensitivity. This dependence directly links tracer magnetic properties to system performance and motivates the use of SPIO which exhibit large nonlinear magnetic susceptibility.

1.3.3 Signal Encoding and Spatial Resolution

To create an image in MPI, information about the spatial distribution of magnetic material must be obtained. The act of including spatial information into the MPI signal is referred to as spatial encoding. In MPI, spatial encoding is achieved through the introduction of a field free region (FFR). The FFR is a region in space with little or no static magnetic field, where SPIOs are free to oscillate in response to the excitation field and therefore contribute strongly to the detected signal. Outside of the FFR, SPIOs experience a static magnetic field which suppress their oscillations, thereby reducing their

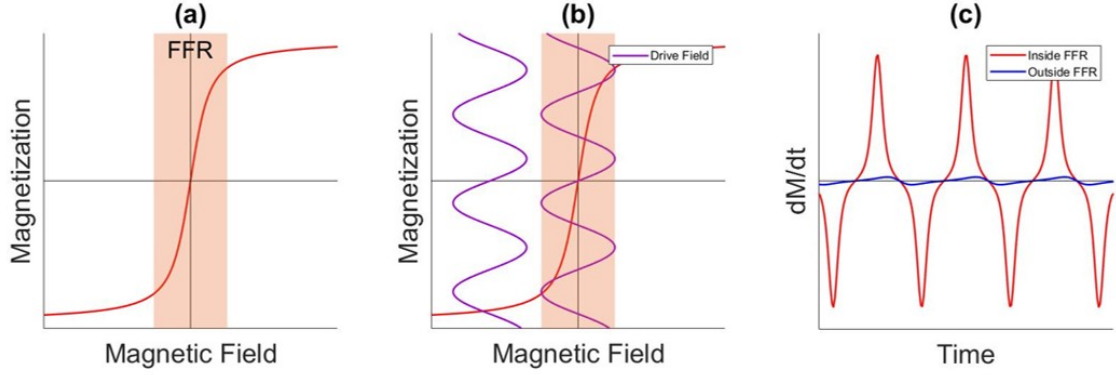


Figure 1.3: **How an FFR introduces spatial encoding.** (a) Magnetization curve for a sample of SPIOs. (b) Application of an oscillating excitation field to samples located at and outside the field free region (FFR). (c) Time derivative of the magnetization when an oscillating excitation field is applied. Note the reduced sensitivity of SPIOs exposed to nonzero static fields outside of the FFR.

contribution to the induced voltage in the receive coil (since $u(t) \propto \partial M / \partial t$). This behavior is illustrated in Fig. 1.3. The FFR thus defines a sensitive region within the imaging volume, and scanning the FFR enables sequential interrogation of different spatial locations.

The FFR is created by applying a magnetic field gradient G , which produces a spatially varying static field of the form $\vec{H}_{\text{sel}}(x) = Gx$, referred to as the selection field. The selection field is typically generated by electromagnetic coils referred to as selection coils. By adjusting the relative currents in these coils, the position of the FFR can be translated throughout the imaging volume, allowing the contents of one region to be measured at a time (discussed in Sec. 2.3).

Ideally, no signal would be produced by SPIOs located outside of the FFR. In practice, however, SPIOs still contribute signal at nonzero offset fields due to the non-infinite susceptibility (i.e. an ensemble of particles takes some non-infinitesimal field to achieve saturation). As shown in Eq. 1.9, the detected MPI signal is proportional to the

field derivative of the magnetization, $\partial M/\partial H$. Figure 1.2 demonstrates that $\partial M/\partial H$ has a nonzero width characterized by its FWHM. The FWHM provides a practical measure of resolvability, because it corresponds to the field separation required for two equal tracer contributions to be distinguishable.

In the presence of a selection field gradient G , the FWHM of $\partial M/\partial H$ can be converted to a spatial resolution Δx :

$$\Delta x \approx \frac{\text{FWHM}}{G}. \quad (1.10)$$

A narrower $\partial M/\partial H$ curve and a stronger gradient therefore lead to improved spatial resolution. This relationship directly links tracer magnetic properties and gradient strength to the achievable spatial resolution in MPI.

1.3.4 Field Free Line vs Field Free Point

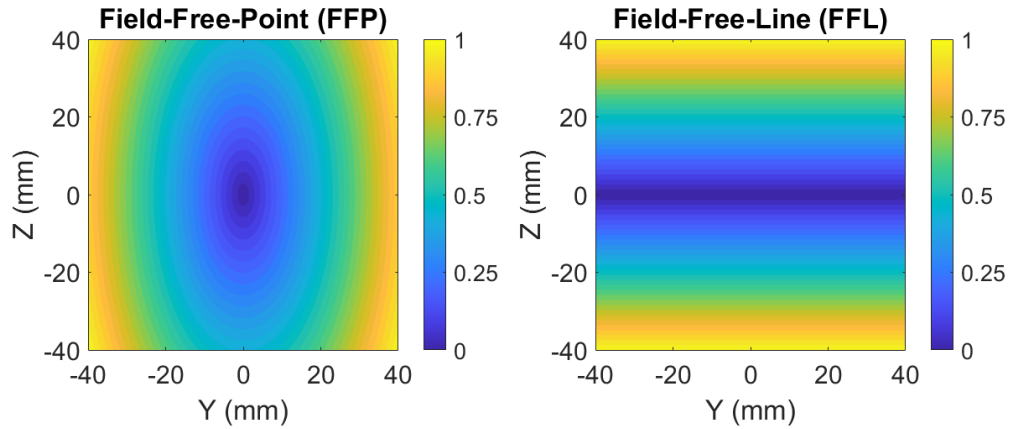


Figure 1.4: **Field free point and field free line selection fields.** Magnetic field magnitude maps illustrating the zero-field regions for an FFP and an FFL selection field.

In MPI two distinct geometries of FFR exist: field free point (FFP) and field free line (FFL), each with their own unique advantages and challenges. Due to the constraints of Maxwell's equations, specifically the constraint $\nabla \cdot \vec{B} = 0$, higher dimensional simple geometries (i.e. field free plane) are nonphysical, and therefore do not exist.

In an FFP scanner [10], the FFR is localized to a single point in space, as illustrated in Fig. 1.4 (left). This configuration enables sampling of individual voxels in space as the FFP is scanned through the imaging volume. In principle, image reconstruction could be performed using simple point-wise mapping approaches. However, in practice such methods are not feasible due to the limited sensitivity associated with single voxel sampling. Consequently, system-function based reconstruction techniques are typically employed to improve sensitivity. These methods require either sophisticated simulations or extensive calibration measurements, which can take many hours and whose accuracy directly determines image fidelity. In addition, system-function approaches are less robust than analytical reconstruction techniques and can produce image artifacts when measurement conditions deviate from those used during calibration, such as during in-vivo imaging.

In an FFL scanner [48], the FFR takes on the geometry of a line segment, as shown in Fig. 1.4 (right). In this case, the detected signal is a summation of all tracer particles located along the line. This geometry is analogous to computed tomography (x-ray), where the measured signal corresponds to a line integral through the object. Consequently, spatial encoding and image reconstruction in an FFL system requires tomographic methods to recover the underlying tracer distribution from multiple projections.

FFL offers several advantages over FFP-based systems, most notably its potential for superior sensitivity. Because the FFL interrogates an extended region of space simultaneously, a larger fraction of the tracer distribution contributes to each measurement compared to point-wise sampling with an FFP, which in turn leads to increased sensitivity.

Additionally, FFL allows access to filtered backprojection (FBP), an analytic image reconstruction technique originally developed for computed tomography. This provides FFL scanners with a robust and computationally efficient reconstruction method allowing for real-time image reconstruction.

However, FFL systems also present inherent challenges. Image formation requires rotation of the FFL relative to the object being imaged, either through mechanical rotation of the scanner, mechanical rotation of the subject, or electronic rotation of the FFL [49]. In a clinical setting, rotation of the patient is undesirable, leaving hardware rotation or electronic rotation of the FFL as the only viable options. Both approaches introduce non-trivial engineering challenges.

1.4 State of the Art

MPI has shown exceptional performance in the preclinical setting, supported by two commercial systems from Bruker and Magnetic Insight, along with numerous research systems [50]–[52]. The field is now in the early stages of transitioning toward human-scale imaging. This transition is non-trivial because scaling hardware to larger volumes requires significantly more power to achieve the same field strengths used in preclinical scanners. These field strengths are necessary to maintain both resolution and sensitivity.

To date, no MPI system has performed in-vivo human imaging. The most advanced demonstrations have been limited to phantom studies, with a single report of imaging in a human cadaver [38], and recent work showing in-vivo imaging of non-human primates (NHP) [53]. No commercially available human scanner exists. Two companies, Magnetic Insight and Mitsubishi, have disclosed development of human-scale scanners, targeting head imaging. However, these devices remain prototypes, are unavailable for purchase, and have only limited technical specifications released.

Consequently, all operational human-scale MPI systems are research prototypes developed by various institutions.

Scaling challenges have motivated the exploration of specialized geometries and targeted anatomical applications. The standard closed-bore design used in preclinical scanners does not scale effectively because increasing bore size reduces achievable field strengths for feasible power consumption. Philips attempted to develop a full-body, closed-bore human MPI system between 2010 and 2015, but ultimately discontinued the effort due to technical and economic constraints [40], [54]. More recent strategies have focused on limiting bore size to specific anatomies, enabling higher field strengths, or on developing alternative scanner topologies.

The most common target is the human head, with scanners typically featuring bore diameters around 20 cm and gradient strengths up to 1 T/m. In addition to the two commercial prototypes, several academic groups are developing head MPI systems [32]–[35]. Notably, the Massachusetts General Hospital group has demonstrated functional brain imaging in NHPs [36], although no head MPI system has yet been tested on a live human subject or cadaver. Another promising approach is the iMPI leg scanner, developed for interventional imaging [38], [39]. This 20 cm bore system achieves a gradient of 0.36 T/m and has imaged catheter coated with SPIO in a cadaver leg for safety studies, but no live human trials have been reported.

Further technical specifications of recent human-scale MPI systems, including gradient strength, drive amplitude, imaging field of view, and sensitivity, are summarized in Table 1.1. These values establish useful performance benchmarks for new scanner designs.

1.4.1 Our Single-Sided Scanner

Single-sided MPI scanners offer a different approach to scaling to human-sized volumes by placing all hardware on one side of the device, allowing open access to the

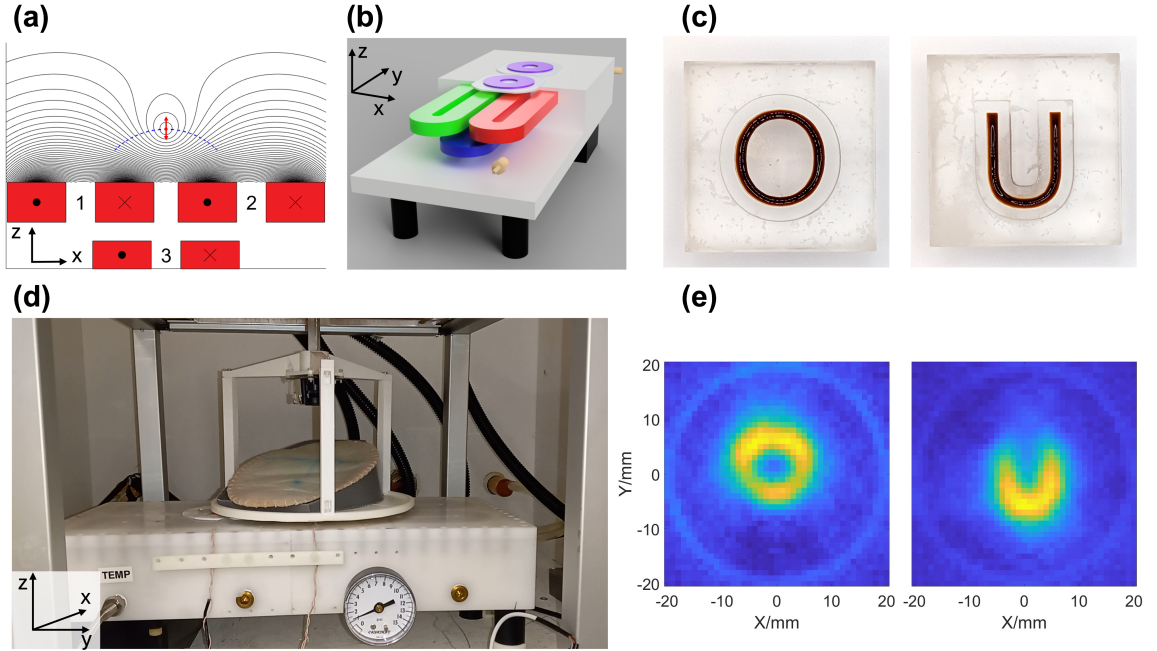


Figure 1.5: Setup of single-sided FFL scanner. **a** Cross-sectional schematic of the single-sided MPI scanner, showing internal coils and magnetic field geometry. Selection coils (1 and 2, red blocks) are positioned on the scanner surface, with the excitation coil (3) located below. Black lines represent the static magnetic field generated by the selection coils, forming an FFL in the center of the scanner (red dot). The dashed blue arc indicates the range of FFL positions achieved by varying the relative currents. Red arrows show the direction of the excitation field. **b** 3D rendering of the scanner assembly. Selection coils (red and green) near the scanner surface, with excitation coil (blue) below them. The receive coil and gradiometer coils (purple) are located on the surface of the scanner. **c** Photograph of two SPIO-filled phantoms shaped as the letters “O” and “U”. **d** Photograph of the experimental setup. A breast phantom is positioned inside a holder in the center of the sample table, which allows for rotation and vertical translation of the subject. **e** Examples of MPI images of “O” and “U” phantoms acquired with our single-sided scanner, demonstrating its ability to image complex geometries.

imaging subject. This configuration provides unrestricted access but produces inhomogeneous magnetic fields, which lead to challenges in image reconstruction as well as limited imaging depth. These characteristics make single-sided scanners well suited for

imaging anatomies attached to larger structures that could not be accommodated in a closed-bore system, such as the breast.

Although multiple single-sided scanners have been developed since the topology was first proposed [41], and others [42], [44], [45], [55], [56], the potential of this approach remains relatively unexplored. Most single-sided scanners exhibit reduced sensitivity, smaller usable fields of view, and non-linear spatial encoding. Our group has developed a single-sided scanner that uses an FFL configuration unique to our design [44], [45], which offers greater sensitivity compared to systems based on an FFP [48], [57]. Our system is the highest-performing and most developed example of this geometry to date [58], and it is intended to advance single-sided MPI into the human imaging regime.

This is the only MPI system specifically designed for breast imaging, combining full tomographic capability with an open geometry unconstrained by bore size, enabling accommodation of subjects of any size. We have demonstrated imaging of an 8 cm field of view within a 20 cm breast phantom, achieving a gradient strength of 1 T/m and a sensitivity of 2 μg of iron, which is competitive with the performance of other human-scale systems listed in Table 1.1.

The design, development, and performance optimization of this scanner are the central focus of this thesis. The following chapters describe the theoretical principles that underpin its operation, the engineering strategies that enabled its performance, and the experimental validation that positions it as a strong candidate for future clinical translation.

Table 1.1: Comparison of human-scale MPI scanner systems.

Scanner Name	Bore Size (cm)	Gradient (T/m)	Drive Amplitude (mT)	Imaging FOV (cm)	Imaging Time (s)	Sensitivity (μg)
Our Single-Sided FFL Scanner [58]	20	1	4	8 x 8 x 1	100	2
iMPI Leg Scanner [38]	20	0.36	35	18 x 14	0.125	10
Hamburg Human Head Scanner [32]	19–25	0.2	6	10 x 14	0.5	8
Superconducting Scanner [34]	20	0.5–2.5	200	10 x 13 x 9.8	50	–
Beijing University NHP Scanner [35]	19	0.25	6	8 x 16 x 8	20–40	19
Massachusetts General Hospital Head Scanner [36]	18–20	1	7	19 x 19	5	1
Magnetic Insight [59]	23	0.6	7	23 x 23 x 6	–	–
Mitsubishi	30	0.3	12	19 x 19	–	–

CHAPTER TWO

PHYSICS & THEORY

2.1 MPI as a small signal detection problem

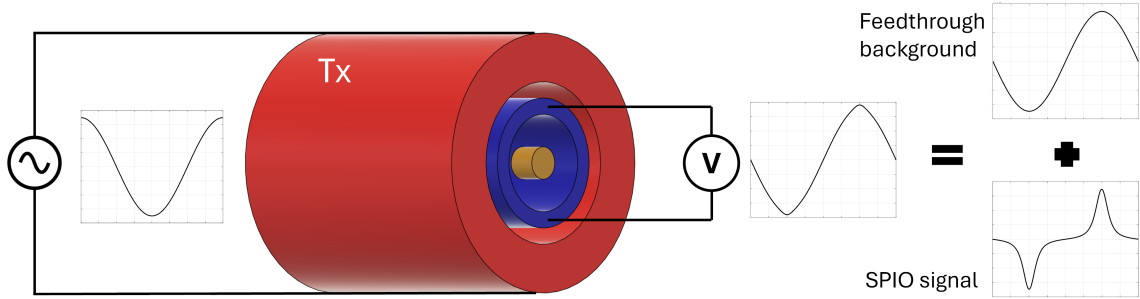


Figure 2.1: **Simplified signal detection in MPI.** A sinusoidal excitation current is applied to the transmit (Tx) coil (red), generating a time varying magnetic field that excites the SPIO sample (orange). The oscillating magnetization of the SPIO sample induces a voltage in the receive (Rx) coil (blue). The measured receive signal consists of both direct feedthrough from the excitation field and the particle-dependent signal arising from the SPIO magnetization. Representative waveforms illustrate the applied excitation, the total signal in the receive coil, the excitation feedthrough, and the signal originating from the SPIO.

MPI can be viewed not only as a biomedical imaging modality, but also as a precision measurement experiment. At its core, MPI involves measuring a weak voltage signal ($<1 \mu\text{V}$) generated by a small quantity of magnetic tracer particles (on the order of $1 \mu\text{g}$ of Fe) in the presence of a much larger background. This signal originates from the nonlinear magnetization of the SPIO tracer particles under excitation by an AC (~ 25 kHz) magnetic field (~ 5 mT), and is detected as an induced voltage in the receive coil according to Faraday's law. However, the same excitation field also directly couples to the

receive coil, producing a large feedthrough signal that often exceeds the tracer-induced voltage by six or more orders of magnitude. As a result, MPI becomes a problem of isolating a small, meaningful physical signal from a dominant and systematic background introduced by the instrumentation itself.

This challenge can be conceptually understood through the following signal pathway:

Transmit field $\rightarrow$ SPIO tracer $\rightarrow$ Receive coil (desired)

Transmit field $\rightarrow$ Receive coil (undesired background)

The induced tracer signal may be smaller than the background by a factor of 10^6 (or more), depending on system geometry, excitation waveform, and SPIO properties. The ability to accurately separate this small signal from the large background directly determines the sensitivity of the system. Sensitivity, in turn, determines the clinical tasks MPI is able to fulfill. With a sensitivity of $1\ \mu\text{g}$, tasks such as tumor detection, functional imaging of the brain, and blood flow imaging are possible. Lowering this sensitivity to $1\ \text{pg}$ or below would allow for tracking of individually labeled cells, which typically uptake roughly $1\text{--}10\ \text{pg}$ of iron per cell [60]. Therefore, careful background subtraction is critical when designing and developing an MPI scanner.

A straightforward strategy for background removal is to perform a background scan without a sample and subtract it from a scan acquired with tracer present. While effective in principle, this approach is limited by the requirement for extreme system stability, and a large bandwidth in the electronics. Given the large disparity in signal magnitude, even a fluctuation on the order of 10^{-6} in the background can obscure the tracer signal entirely. Therefore, background subtraction alone is rarely sufficient, and

additional techniques must be employed to suppress the background and improve overall sensitivity.

A variety of strategies spanning hardware, data acquisition, and signal processing are used to address this challenge. On the hardware side, techniques such as the use of receive gradiometer coils can attenuate common mode feedthrough. On the signal processing side, methods that exploit the spectral characteristics of the SPIO response, such as harmonic filtering and lock-in detection, can selectively isolate signal components unique to the tracer. These techniques are used in combination, often implemented iteratively, to incrementally improve the sensitivity of the system.

Viewed in this way, MPI resembles other precision experiments in experimental physics, such as those in particle detection or gravitational wave measurement, where the central challenge is detecting small signals on a large background through increasingly careful control of the measurement apparatus. The scanner developed in this work was designed within this framework. Its receive coil design, filter architecture, and data acquisition protocols reflect an iterative process of refinement aimed at reducing background and improving signal fidelity. Many of the design decisions in this work contributes to the broader goal of pushing the MPI sensitivity of our system toward clinically meaningful regimes.

2.2 Field-Free Line Generation

In MPI the field-free region (FFR) defines where particles are unsaturated and therefore contribute to the received signal. Our scanner employs a field-free line (FFL), generated by electromagnetic coils (termed selection coils), as the basis for spatial encoding. The ability to generate and control the position of the FFL is central to imaging, since it defines the region of sensitivity to the SPIO tracer.

The selection coils in our system are racetrack-shaped windings elongated along the y -axis, with a rectangular cross section in the xz plane (Fig. 2.2). This elongated

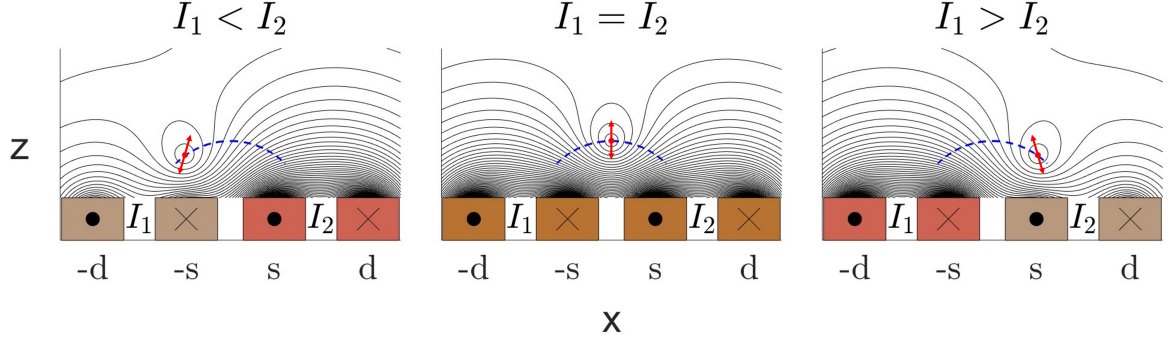


Figure 2.2: **FFL generation schematic.** Diagram of single-sided FFL selection coils. The xz -contour plot of the magnetic field shows the FFL above the coil surface generated by a pair of coils. The FFL position and excitation direction at the location of the FFL are shown in red, with the trajectory of the FFL indicated by the dashed blue arc.

geometry ensures that the FFL is effectively invariant along y , so that the magnetic field depends only on x and z ($B_{\text{sel}}(x, y, z) = B_{\text{sel}}(x, z)$). By applying DC currents to the selection coils, the FFL is formed at a height above the scanner surface with a controllable lateral (x) position. Adjusting the relative currents allows the FFL to be shifted electronically within the FOV.

The principle of FFL generation can be illustrated using a simplified model of four parallel, infinitely long conductors, which represent two racetrack coils. The pair of conductors on the left is driven with equal and opposite currents I_1 , while the pair on the right is driven with equal and opposite currents I_2 . Using the Biot–Savart law, the field from the left pair is

$$\mathbf{B}_{\text{left}}(x, z) = \frac{\mu_0 I_1}{2\pi} \left[\left(\frac{z}{(x+d)^2 + z^2} - \frac{z}{(x+s)^2 + z^2} \right) \hat{\mathbf{x}} + \left(\frac{x+s}{(x+s)^2 + z^2} - \frac{x+d}{(x+d)^2 + z^2} \right) \hat{\mathbf{z}} \right], \quad (2.1)$$

where d is the x -position of the outer conductor, and s is the x -position of the inner conductor. The right pair produces a similar field,

$$\mathbf{B}_{\text{right}}(x, z) = \frac{\mu_0 I_2}{2\pi} \left[\left(\frac{z}{(x-s)^2 + z^2} - \frac{z}{(x-d)^2 + z^2} \right) \hat{\mathbf{x}} + \left(\frac{x-d}{(x-d)^2 + z^2} - \frac{x-s}{(x-s)^2 + z^2} \right) \hat{\mathbf{z}} \right]. \quad (2.2)$$

The total selection field is the sum,

$$\mathbf{B}_{\text{sel}}(x, z) = \mathbf{B}_{\text{left}}(x, z) + \mathbf{B}_{\text{right}}(x, z).$$

When the coil currents are equal, $I_1 = I_2 = I$, the x -component of the field cancels along $x = 0$, leaving only the z -component:

$$\mathbf{B}_{\text{sel}}(x = 0, z) = \frac{\mu_0 I}{\pi} \left(\frac{s}{s^2 + z^2} - \frac{d}{d^2 + z^2} \right) \hat{\mathbf{z}}. \quad (2.3)$$

The FFL occurs where this field vanishes along the y -direction,

$$\mathbf{B}_{\text{sel}}(x = 0, y, z = h) = 0,$$

which gives

$$h = \sqrt{sd}.$$

Thus, equal currents in the two selection coils generate an FFL centered at $x = 0$ and height $z = h$. By varying the relative currents I_1 and I_2 , the FFL can be shifted laterally (x) across the FOV. This controllability is the basis of spatial encoding in our scanner and provides the foundation for the discrete stepping method described in the next section.

2.3 Discrete Stepping MPI

The previous section described how the FFL is generated and positioned by applying controlled currents to the selection coils. In practice, spatial encoding requires that the FFL be scanned across the entire FOV so that signals from all regions can be acquired. In conventional closed-bore MPI systems, sinusoidal drive currents applied to

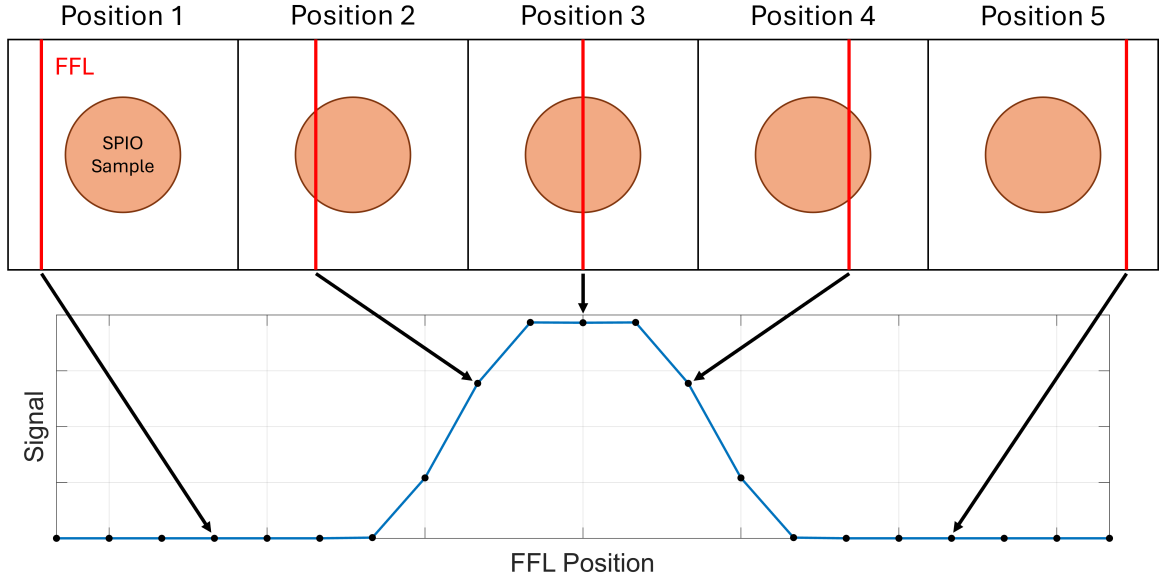


Figure 2.3: **Discrete stepping MPI diagram.** Schematic illustrating the discrete stepping acquisition method used in this work. The FFL (red) is sequentially positioned at discrete locations along the x -direction across an SPIO sample (orange), at each location the signal is recorded. Plotting the measured signal amplitude as a function of FFL position yields a projection of the tracer distribution. This schematic assumes that the FFL remains at a constant height in the z -direction during the scan.

the selection coils generate Lissajous trajectories of the FFR. These trajectories provide predictable coverage of the imaging FOV due to their homogeneous selection fields.

However, in a single-sided geometry, the selection fields are inhomogeneous. Therefore, applying sinusoidal currents no longer produces a standard Lissajous trajectory, and the resulting FFL motion is nonlinear and does not guarantee coverage of the imaging FOV.

To address this, our system employs a discrete stepping approach, illustrated schematically in Fig. 2.3. The FFL is first formed above the scanner surface along the y -axis, with a specified x and z coordinate determined by the relative currents applied to the selection coils. Two algorithms were developed to calculate the currents required to place the FFL at a given x location, each described in detail later in this work. The scan

begins with the FFL positioned at one edge of the FOV. After a brief stabilization period to allow switching transients to decay, the signal is recorded for a fixed acquisition window (typically ~ 90 ms). The FFL is then stepped to the next position, separated by a variable step in the x-direction, where the stabilization–acquisition cycle is repeated. A typical scan involves 41 such steps, providing a one-dimensional projection of the object along x at a defined height z. This discrete stepping approach is unique to our scanner, but it is conceptually related to x-space MPI [50] in that time-series data are associated with specific spatial locations, although in our case the FFL is moved in a discrete rather than continuous manner.

The main advantages of discrete encoding are its robustness, ease of implementation, and the ability to temporally separate selection coil feedthrough from the SPIO signal, which makes it particularly well suited for system prototyping. The primary drawback is that time is lost while waiting for transients to decay. Continuous FFL motion could in principle improve SNR by eliminating these idle periods, but the theoretical gain is modest. With current timing parameters (90 ms acquisition, ~ 45 ms stabilization), the maximum possible sensitivity improvement would be a factor of $\sqrt{135/90} \approx 1.2$. Furthermore, continuous scanning would require complex nonlinear drive waveforms due to inhomogeneous fields, and feedthrough could no longer be isolated temporally, introducing additional background. For these reasons, while continuous scanning is feasible in principle, the discrete approach provides a more practical and reliable solution for the present prototype.

2.3.1 Signal Equation

The FFL is generated by at least two independent selection coils, each supplied with a controllable current I_1, I_2 . In the original implementation of our scanner two coils were used, while in a later iteration three coils were employed. The static selection field

during a discrete step is therefore

$$\mathbf{B}_{\text{sel}}(\mathbf{r}, I_1, I_2, I_3) = I_1 \mathbf{P}_1(\mathbf{r}) + I_2 \mathbf{P}_2(\mathbf{r}) + I_3 \mathbf{P}_3(\mathbf{r}), \quad (2.4)$$

where $\mathbf{P}_i(\mathbf{r})$ is the field produced by selection coil i at unit current. During data acquisition this field is time-independent, and the FFL position is set by the relative values of I_1 and I_2 (and I_3 if present). Therefore, $\mathbf{B}_{\text{sel}}$ can be defined as a function of FFL position ($\mathbf{r}_{\text{FFL}}$) $B_{\text{sel}}(\mathbf{r}, I_1, I_2, I_3) = B_{\text{sel}}(\mathbf{r}, \mathbf{r}_{\text{FFL}})$.

Superimposed on this static field is the oscillating excitation field generated by the excitation coil at $\omega_1 = 25$ kHz,

$$\mathbf{B}_{\text{ex}}(\mathbf{r}, t) = I_{\text{peak}} \cos(\omega_1 t) \mathbf{P}_{\text{ex}}(\mathbf{r}). \quad (2.5)$$

The total field and its time derivative are

$$\mathbf{B}(\mathbf{r}, \mathbf{r}_{\text{FFL}}, t) = \mathbf{B}_{\text{sel}}(\mathbf{r}, \mathbf{r}_{\text{FFL}}) + \mathbf{B}_{\text{ex}}(\mathbf{r}, t), \quad \frac{\partial \mathbf{B}}{\partial t}(\mathbf{r}, t) = -\omega_1 I_{\text{peak}} \sin(\omega_1 t) \mathbf{P}_{\text{ex}}(\mathbf{r}). \quad (2.6)$$

The Langevin model describes the magnetization of the SPIOs (see Eq.1.1),

$$\mathbf{M}(\mathbf{r}, t) = c(\mathbf{r}) m \mathcal{L}(\xi(t)) \hat{\mathbf{B}}(t), \quad \xi(t) = \frac{m}{k_B T} |\mathbf{B}(\mathbf{r}, t)|, \quad \hat{\mathbf{B}}(t) = \frac{\mathbf{B}(\mathbf{r}, t)}{|\mathbf{B}(\mathbf{r}, t)|}. \quad (2.7)$$

Differentiating gives

$$\frac{\partial \mathbf{M}}{\partial t} = c(\mathbf{r}) m \left[\mathcal{L}'(\xi) \frac{m}{k_B T} (\hat{\mathbf{B}} \cdot \frac{\partial \mathbf{B}}{\partial t}) \hat{\mathbf{B}} + \mathcal{L}(\xi) \frac{1}{|\mathbf{B}|} \left(\frac{\partial \mathbf{B}}{\partial t} - (\hat{\mathbf{B}} \cdot \frac{\partial \mathbf{B}}{\partial t}) \hat{\mathbf{B}} \right) \right]. \quad (2.8)$$

The receive coil measures the induced voltage,

$$u(\mathbf{r}_{\text{FFL}}, t) = - \int \mathbf{P}_{\text{rx}}(\mathbf{r}) \cdot \frac{\partial \mathbf{M}(\mathbf{r}, t)}{\partial t} dV, \quad (2.9)$$

where $\mathbf{P}_{\text{rx}}(\mathbf{r})$ is the sensitivity of the receive coil.

2.3.2 Convolution and Pseudo-Convolution

Since the goal of MPI is to recover the spatial distribution of SPIOs, it is helpful to rewrite the signal equation in terms of the concentration $c(\mathbf{r})$. To do this, we define the concentration-independent magnetization

$$\mathbf{M}_0(\mathbf{r}, t) = \frac{\mathbf{M}(\mathbf{r}, t)}{c(\mathbf{r})}, \quad (2.10)$$

so that

$$\frac{\partial \mathbf{M}}{\partial t} = c(\mathbf{r}) \frac{\partial \mathbf{M}_0}{\partial t}. \quad (2.11)$$

Substituting this expression into the received signal gives

$$u(\mathbf{r}_{\text{FFL}}, t) = - \int c(\mathbf{r}) \mathbf{P}_{\text{rx}}(\mathbf{r}) \cdot \frac{\partial \mathbf{M}_0(\mathbf{r}, t)}{\partial t} dV. \quad (2.12)$$

It is natural to define the system function

$$h(\mathbf{r}, \mathbf{r}_{\text{FFL}}, t) = \mathbf{P}_{\text{rx}}(\mathbf{r}) \cdot \frac{\partial \mathbf{M}_0(\mathbf{r}, \mathbf{r}_{\text{FFL}}, t)}{\partial t}, \quad (2.13)$$

so that the measured voltage becomes

$$u(\mathbf{r}_{\text{FFL}}, t) = - \int c(\mathbf{r}) h(\mathbf{r}, \mathbf{r}_{\text{FFL}}, t) dV. \quad (2.14)$$

The system function $h(\mathbf{r}, \mathbf{r}_{\text{FFL}}, t)$ incorporates the excitation, receive, and selection field profiles together with the SPIO particle physics, and thus describes how the tracer distribution contributes to the measured voltage at each FFL position.

In the special case where the excitation and selection fields are homogeneous, $h(\mathbf{r}, \mathbf{r}_{\text{FFL}}, t)$ depends only on the relative displacement from the FFL position:

$$h(\mathbf{r}, \mathbf{r}_{\text{FFL}}, t) = h(\mathbf{r} - \mathbf{r}_{\text{FFL}}, t). \quad (2.15)$$

Equation 2.14 then reduces to a true convolution,

$$u(\mathbf{r}_{\text{FFL}}, t) = - \int c(\mathbf{r}) h(\mathbf{r} - \mathbf{r}_{\text{FFL}}, t) dV = - [c(\mathbf{r}) * h(\mathbf{r}, t)], \quad (2.16)$$

with $h(\mathbf{r}, t)$ acting as the point spread function (PSF). In this regime, image reconstruction is equivalent to deconvolution, as in x-space MPI [61], [62].

In a single-sided geometry, however, the selection fields are inhomogeneous, and h depends explicitly on both $\mathbf{r}$ and $\mathbf{r}_{\text{FFL}}$. In this case Eq. 2.14 is a pseudo-convolution, and direct deconvolution cannot be applied. Instead, calibration-based or model-based linear algebra approaches can be employed to account for the spatial variation of the system function.

2.3.3 Simplifications of Signal Equation

The general form of the discrete stepping MPI signal equation (Eq. 2.12) contains several terms that are difficult to interpret directly. To gain physical intuition, it is useful to consider limiting cases where the expression simplifies. These limits reveal the dependencies of the signal on experimental parameters, tracer properties, and applied fields.

2.3.3.1 Zero DC Field Simplification An important special case is when the SPIO sample is exposed to zero DC offset field $\mathbf{B}_{\text{sel}}(\mathbf{r} = \mathbf{r}_{\text{SPIO}}) = 0$. This situation arises when the SPIOs are located at the FFL, or in systems that operate without a selection field such as magnetic particle spectrometers (MPS). In this case the total field reduces to $\mathbf{B} = \mathbf{B}_{\text{ex}}$, and its direction $\hat{\mathbf{B}}$ is fixed by the excitation coil profile $\mathbf{P}_{\text{ex}}(\mathbf{r})$. As a result, only the parallel contribution remains in Eq. 2.8, and the time derivative of the magnetization becomes

$$\frac{\partial \mathbf{M}}{\partial t} = -\omega_1 I_{\text{peak}} \sin(\omega_1 t) c(\mathbf{r}) m \mathcal{L}'(\xi(\mathbf{r}, t)) \frac{m}{k_B T} |\mathbf{P}_{\text{ex}}(\mathbf{r})| \hat{\mathbf{B}}_{\text{ex}}, \quad (2.17)$$

where $\xi(\mathbf{r}, t) = \frac{m}{k_B T} |\mathbf{B}_{\text{ex}}(\mathbf{r}, t)|$. The induced receive voltage is then

$$u(t) = \frac{m^2 \omega_1 I_{\text{peak}}}{k_B T} \sin(\omega_1 t) \int c(\mathbf{r}) \mathcal{L}'(\xi(\mathbf{r}, t)) |\mathbf{P}_{\text{ex}}(\mathbf{r})| (\mathbf{P}_{\text{rx}}(\mathbf{r}) \cdot \hat{\mathbf{B}}_{\text{ex}}(\mathbf{r})) dV. \quad (2.18)$$

This expression highlights several important features. First, the signal amplitude scales linearly with the excitation frequency ω_1 , meaning that higher-frequency excitation fields yield proportionally stronger signals. Second, the signal is proportional to m^2 , showing that the single-particle magnetic moment has a strong influence on signal.

2.3.3.2 Weak-Excitation Limit Another useful limit is when the selection field is much larger than the excitation field, $|\mathbf{B}_{\text{sel}}| \gg |\mathbf{B}_{\text{ex}}|$. Because the selection field must vanish at the FFL, this approximation cannot hold over the entire FOV, but it is valid for SPIOs located far from the FFL where the static field dominates. In this regime the total field is nearly constant, $|\mathbf{B}| \approx |\mathbf{B}_{\text{sel}}|$, and aligned with $\hat{\mathbf{B}}_{\text{sel}}$, so the perpendicular contribution in Eq. 2.8 is negligible:

$$\frac{\partial \mathbf{M}}{\partial t} \approx -\omega_1 I_{\text{peak}} \sin(\omega_1 t) c m \mathcal{L}'(\xi_0(\mathbf{r})) \frac{m}{k_B T} (\hat{\mathbf{B}}_{\text{sel}}(\mathbf{r}) \cdot \mathbf{P}_{\text{ex}}(\mathbf{r})) \hat{\mathbf{B}}_{\text{sel}}, \quad (2.19)$$

with $\xi_0(\mathbf{r}) = \frac{m}{k_B T} |\mathbf{B}_{\text{sel}}(\mathbf{r})|$. The corresponding induced voltage is

$$u(\mathbf{r}_{\text{FFL}}, t) \approx \frac{m^2 \omega_1 I_{\text{peak}}}{k_B T} \sin(\omega_1 t) \int c(\mathbf{r}) \mathcal{L}'(\xi_0(\mathbf{r})) (\hat{\mathbf{B}}_{\text{sel}}(\mathbf{r}) \cdot \mathbf{P}_{\text{ex}}(\mathbf{r})) (\mathbf{P}_{\text{rx}}(\mathbf{r}) \cdot \hat{\mathbf{B}}_{\text{sel}}(\mathbf{r})) dV. \quad (2.20)$$

In this limit the signal is proportional to the derivative of the Langevin function evaluated at the local selection field strength ξ_0 , implying that the point spread function

takes the form of $\mathcal{L}'(\xi_0)$. Since the only remaining time dependence is the sinusoidal factor $\sin(\omega_1 t)$, the tracer response far from the FFL is effectively linear.

2.4 Narrowband Imaging

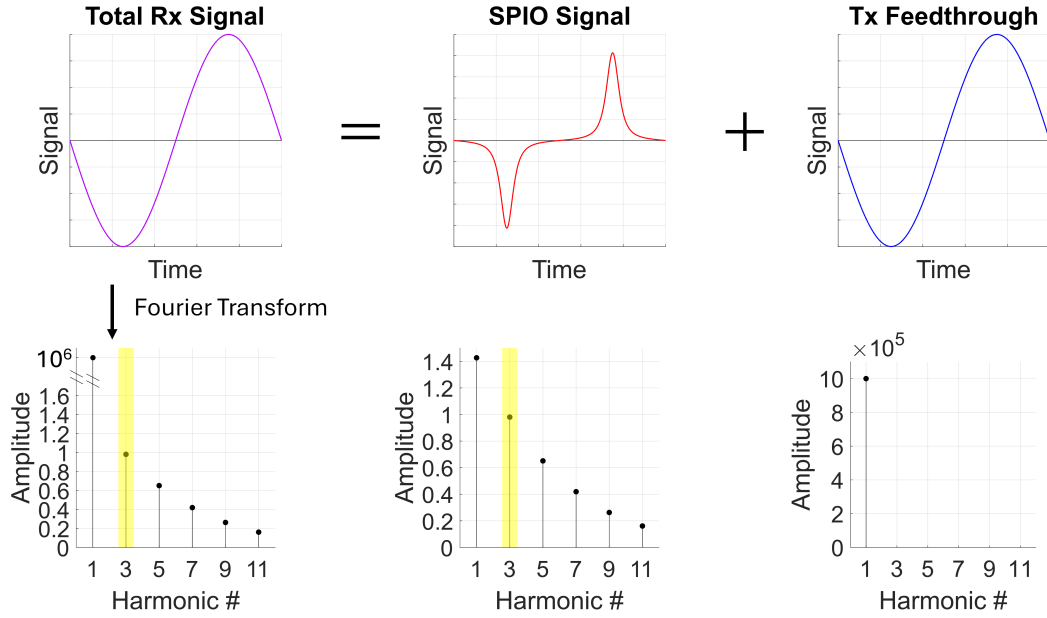


Figure 2.4: **Narrowband signal separation in MPI.** Top row: time domain receive signal decomposition. The total receive signal (left) is the sum of the SPIO induced signal (center) and the excitation feedthrough (right). The total signal is dominated by excitation feedthrough, making direct detection of the SPIO response challenging in the time domain. Bottom row: corresponding Fourier spectra. The excitation feedthrough spectrum is confined to a single frequency (ideally), while the SPIO signal spectra contains odd harmonics of the applied frequency. Consequently, the higher harmonics of the total receive signal are dominated by tracer signal. Narrowband detection exploits this separation by isolating a single higher harmonic, typically the third harmonic (highlighted in yellow), which is the highest amplitude harmonic outside the fundamental.

In MPI the receive signal consists of two components: the tracer-generated response from the nonlinear SPIO magnetization (Eq. 2.12), and the large background

feedthrough from the excitation field. The latter is typically several orders of magnitude stronger ($\sim 10^6$) than the tracer signal, making separation challenging. This feedthrough is unavoidable because the excitation and receive coils must be coaxial, since the SPIOs must be driven along the same axis as the receive coil sensitivity. The useful tracer signal can be distinguished by analyzing the Fourier spectrum of the received voltage (Fig. 2.4). Ideally the feedthrough background power should be entirely constrained to the fundamental frequency (ω_1), since the coil is driven with a pure sinusoid. In contrast, the tracer magnetization produces higher-order odd harmonics of the fundamental¹, owing to the nonlinear Langevin response.

Therefore, separating the signal into its harmonic components provides a practical means of distinguishing the tracer response from excitation feedthrough. While multiple strategies exist for selecting which harmonics to measure and how to combine them into a signal, this work focuses on forming the signal from a single harmonic amplitude, which is commonly referred to as narrowband imaging [63]. In this work we focus on the third harmonic amplitude, since it is the strongest tracer generated harmonic that is not obscured by the large background at the fundamental, providing the highest SNR of the options available.

The main advantage of narrowband imaging is its robustness and simplicity. By focusing on a single frequency, the tracer signal can be measured with a lock-in amplifier, which is optimized for detecting weak signals at a specified frequency even in the presence of a large background. Restricting detection to the third harmonic also removes the time dependence of the signal, leaving only its amplitude as a function of FFL position. Another important advantage is that narrowband imaging requires no assumptions about the tracer environment, the measurement remains valid *in vivo* without relying on calibration data acquired under different conditions. In contrast,

¹A formal proof is provided in the Appendix A.4

multi-harmonic approaches require combining information from several harmonics through linear algebra methods, which depend on calibration and may fail if the physical environment differs between calibration and imaging.

In the following subsections we first derive the harmonic signal equation and identify the contribution of different harmonics, then explore a numeric form for the third harmonic PSF, and finally discuss the limitations of narrowband imaging, including side lobes in the PSF and the loss of SNR and resolution from discarding higher harmonics.

2.4.1 Harmonic Signal Equation

The narrowband signal model is obtained by decomposing the general discrete stepping MPI signal equation (Eq. 2.12) into its Fourier components. For an FFL fixed at position $\mathbf{r}_{\text{FFL}}$, the voltage in the receive coil $u(\mathbf{r}_{\text{FFL}}, t)$ is periodic with the excitation frequency ω_1 . It can therefore be expanded as a Fourier series,

$$u(\mathbf{r}_{\text{FFL}}, t) = \sum_{n=-\infty}^{\infty} U_n(\mathbf{r}_{\text{FFL}}) e^{in\omega_1 t}, \quad (2.21)$$

where $U_n(\mathbf{r}_{\text{FFL}})$ are the complex harmonic amplitudes. Equivalently, each harmonic can be written as a Fourier coefficient of the time domain signal,

$$U_n(\mathbf{r}_{\text{FFL}}) = \frac{\omega_1}{2\pi} \int_{-\pi/\omega_1}^{\pi/\omega_1} u(\mathbf{r}_{\text{FFL}}, t) e^{-in\omega_1 t} dt. \quad (2.22)$$

Here $u(\mathbf{r}_{\text{FFL}}, t)$ is given by Eq. 2.12, with the time dependence entering through $\frac{\partial \mathbf{M}}{\partial t}$ (Eq. 2.8). In general this expression is too complex for analytic Fourier analysis, so we introduce simplifying assumptions to expose the harmonic structure. Assume (i) the magnetization is aligned with the receive-coil sensitivity so that $\frac{\partial \mathbf{M}}{\partial t} \cdot \mathbf{P}_{\text{rx}} = \frac{\partial M}{\partial t} P_{\text{rx}}$, and (ii) both excitation and receive sensitivity are spatially homogeneous with no selection field ($\mathbf{B}_{\text{sel}} = 0$). In this case

$$u(\mathbf{r}_{\text{FFL}}, t) = - \int \mathbf{P}_{\text{rx}} \cdot \frac{\partial \mathbf{M}}{\partial t} dV = -P_{\text{rx}} V \frac{\partial M}{\partial t}(t), \quad (2.23)$$

where V is the tracer volume. The entire time dependence therefore comes from $\frac{\partial M}{\partial t}$.

From the zero selection simplification (Sec. 2.3.3.1), the magnetization derivative reduces to

$$\frac{\partial M}{\partial t} = -\omega_1 c \frac{B_{\text{ex}} m^2}{k_B T} \sin(\omega_1 t) \mathcal{L}'\left(\frac{m B_{\text{ex}}}{k_B T} \cos(\omega_1 t)\right), \quad (2.24)$$

where $B_{\text{ex}} = I_{\text{peak}} P_{\text{ex}}$ is the excitation amplitude. Substituting Eq. 2.24 into Eq. 2.22 gives

$$U_n = \frac{\omega_1^2}{2\pi} \frac{m^2 B_{\text{ex}}}{k_B T} c V P_{\text{rx}} \int_{-\pi/\omega_1}^{\pi/\omega_1} \sin(\omega_1 t) \mathcal{L}'\left(\frac{m B_{\text{ex}}}{k_B T} \cos(\omega_1 t)\right) e^{-in\omega_1 t} dt. \quad (2.25)$$

We can simplify the integral with the substitution $\theta = \omega_1 t$, yielding

$$U_n = \frac{\omega_1}{2\pi} \frac{m^2 B_{\text{ex}}}{k_B T} c V P_{\text{rx}} \int_{-\pi}^{\pi} \sin(\theta) \mathcal{L}'\left(\frac{m B_{\text{ex}}}{k_B T} \cos(\theta)\right) e^{-in\theta} d\theta. \quad (2.26)$$

The harmonic structure comes from the product $\sin(\theta) \mathcal{L}'(\alpha \cos \theta)$, where $\alpha = m B_{\text{ex}} / k_B T$. To analyze this, consider

$$I_n(\alpha) = \int_{-\pi}^{\pi} \sin(\theta) \mathcal{L}'(\alpha \cos \theta) e^{-in\theta} d\theta. \quad (2.27)$$

Writing $e^{-in\theta} = \cos(n\theta) - i \sin(n\theta)$ gives

$$I_n(\alpha) = \int_{-\pi}^{\pi} \sin(\theta) \mathcal{L}'(\alpha \cos \theta) \cos(n\theta) d\theta - i \int_{-\pi}^{\pi} \sin(\theta) \mathcal{L}'(\alpha \cos \theta) \sin(n\theta) d\theta. \quad (2.28)$$

The first integral vanishes because the integrand is an odd function over a symmetric interval. Thus,

$$I_n(\alpha) = -i \int_{-\pi}^{\pi} \sin(\theta) \mathcal{L}'(\alpha \cos \theta) \sin(n\theta) d\theta. \quad (2.29)$$

From symmetry considerations, this integral is zero whenever n is even. Therefore, only odd harmonics contribute to the signal, consistent with the odd-power expansion of the Langevin function. The factor of $-i$ implies that the SPIO signal has a -90° phase shift relative to the excitation. Unfortunately this integral cannot be expressed in closed form for arbitrary α , and must be evaluated numerically. The most compact general expression for the n^{th} harmonic amplitude is

$$U_n = \frac{\omega_1}{2\pi} \frac{m^2 B_{\text{ex}}}{k_B T} c V P_{\text{rx}} I_n\left(\frac{m B_{\text{ex}}}{k_B T}\right). \quad (2.30)$$

For narrowband signal detection we focus on the case $n = 3$, since this is the strongest harmonic that does not overlap with the large feedthrough from the excitation coil:

$$U_3 = \frac{\omega_1}{2\pi} \frac{m^2 B_{\text{ex}}}{k_B T} c V P_{\text{rx}} \int_{-\pi}^{\pi} \sin(\theta) \mathcal{L}'(\alpha \cos \theta) \sin(3\theta) d\theta. \quad (2.31)$$

This integral has no closed form solution for arbitrary α , but it can be evaluated numerically or approximated by expanding $\mathcal{L}'(\alpha \cos \theta)$. Several dependencies are evident from the prefactors. The third harmonic amplitude scales linearly with excitation frequency ω_1 , receive sensitivity P_{rx} , and the total tracer amount cV . In addition, it contains at least a quadratic dependence (m^2) on the particle magnetic moment m , a linear dependence on the excitation amplitude B_{ex} , and an inverse dependence ($1/T$) on temperature T . Additional factors of m^2 , B_{ex} , and $1/T$ may arise from the integral from the dimensionless parameter α , depending on the excitation regime. Thus, while the exact scaling with m , B_{ex} , and T must be determined numerically, the qualitative result is that

stronger drive fields and larger particle moments increase the signal, with the dependence on m being stronger, whereas higher temperatures reduce it. Since lowering temperature is not viable in vivo, improvements in sensitivity must come from increased excitation amplitude, optimized tracer properties, and improved receive sensitivity.

2.4.2 Third-Harmonic Point Spread Function

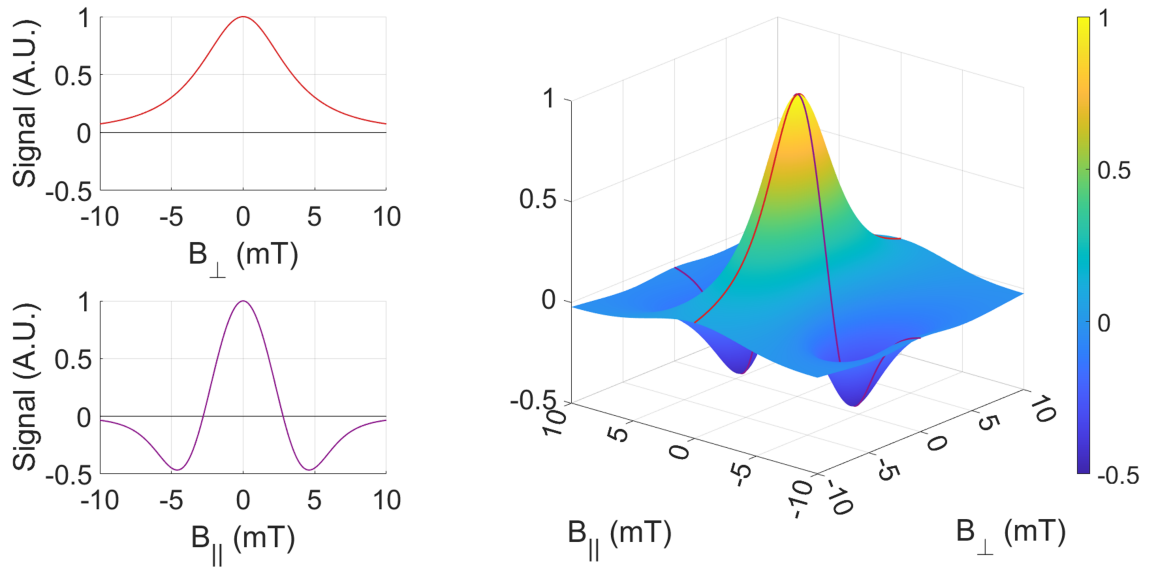


Figure 2.5: **Third-harmonic point spread function.** Numerically evaluated point spread function (PSF) for narrowband MPI using third-harmonic signal detection. Right: 2D PSF as a function of static offset magnetic fields applied perpendicular ($B_{\perp}$) and parallel ($B_{\parallel}$) to the Tx-Rx direction. Left: 1D PSF profiles along the perpendicular (top) and parallel (bottom) directions, obtained by taking central slices through the 2D PSF. The perpendicular PSF exhibits a single dominant positive lobe with a bell-shaped profile, while the parallel PSF displays a sharper central lobe with two negative side lobes.

The point spread function (PSF) describes the signal measured when imaging a point source with a given imaging system. In the ideal case, the PSF is a delta function,

such that signal is only obtained when the detector or sensitive region is sampling the spatial location of said point source. However, due to the physical nature of real imaging systems, this ideal behavior is never achieved. Instead, practical PSFs have thickness, supplying signal when the sensitive region is near the point source, often taking bell-shaped profiles. The shape of the PSF is important, as it governs spatial resolution, image artifacts, and the conditioning of the inverse problem. The goal of this section is to explore the PSF in narrowband MPI from a theoretical perspective.

In narrowband MPI, there is no analytical expression for the PSF, even under extremely simplified assumptions. As a result, the PSF must be analyzed numerically and interpreted qualitatively. The purpose of this section is to outline the numerical approach used to compute the PSF and to analyze its resulting structure. Starting from the general discrete stepping signal equation (Eq. 2.12), the n^{th} harmonic amplitude at a fixed FFL position is obtained by applying the Fourier coefficient operator (Eq. 2.22) to the receive signal $u(\mathbf{r}_{\text{FFL}}, t)$. Substituting Eq. 2.12 into Eq. 2.22 gives

$$U_n(\mathbf{r}_{\text{FFL}}) = - \int c(\mathbf{r}) h_n(\mathbf{r}, \mathbf{r}_{\text{FFL}}) dV, \quad (2.32)$$

where the harmonic system function is defined as

$$h_n(\mathbf{r}, \mathbf{r}_{\text{FFL}}) = \frac{\omega_1}{2\pi} \int_{-\pi/\omega_1}^{\pi/\omega_1} \mathbf{P}_{\text{rx}}(\mathbf{r}) \cdot \frac{\partial \mathbf{M}_0(\mathbf{r}, \mathbf{r}_{\text{FFL}}, t)}{\partial t} e^{-in\omega_1 t} dt. \quad (2.33)$$

Equation 2.32 makes the PSF interpretation explicit. For a point like tracer distribution, $c(\mathbf{r}) = c_0 \delta(\mathbf{r} - \mathbf{r}_0)$, the harmonic signal reduces to

$$U_n(\mathbf{r}_{\text{FFL}}; \mathbf{r}_0) = -c_0 h_n(\mathbf{r}_0, \mathbf{r}_{\text{FFL}}), \quad (2.34)$$

so the harmonic PSF for a point located at $\mathbf{r}_0$ is directly proportional to $h_n(\mathbf{r}_0, \mathbf{r}_{\text{FFL}})$ viewed as a function of the scan coordinate $\mathbf{r}_{\text{FFL}}$.

For narrowband imaging we consider $n = 3$, and define the third-harmonic PSF as

$$\text{PSF}_3(\mathbf{r}_{\text{FFL}}; \mathbf{r}_0) \propto h_3(\mathbf{r}_0, \mathbf{r}_{\text{FFL}}). \quad (2.35)$$

Rather than parameterizing the PSF directly in terms of spatial coordinates, it is more convenient to express it as a function of static offset magnetic fields, since spatial encoding is achieved by applying a gradient magnetic field. For a point tracer located at $\mathbf{r}_0$, the selection field at that location during a discrete step acts as an effective DC offset, $\mathbf{B}_{\text{DC}} = \mathbf{B}_{\text{sel}}(\mathbf{r}_0, \mathbf{r}_{\text{FFL}})$. Decomposing this offset into components parallel and perpendicular to the excitation and receive sensitivity direction yields

$$\mathbf{B}_{\text{DC}} = B_{\parallel} \hat{\mathbf{e}}_{\parallel} + B_{\perp} \hat{\mathbf{e}}_{\perp}. \quad (2.36)$$

The third-harmonic PSF may then be evaluated by sweeping $(B_{\parallel}, B_{\perp})$ and computing the resulting third-harmonic signal amplitude,

$$\text{PSF}_3(B_{\parallel}, B_{\perp}) \propto U_3(B_{\parallel}, B_{\perp}), \quad (2.37)$$

where U_3 is obtained numerically by evaluating Eq. 2.33 using the full magnetization derivative (Eq. 2.8) with total applied field $\mathbf{B}(t) = \mathbf{B}_{\text{DC}} + \mathbf{B}_{\text{ex}}(t)$.

Figure 2.5 shows the numerically evaluated third-harmonic PSF as a function of $(B_{\parallel}, B_{\perp})$, together with one-dimensional cuts through the center of the distribution. Along the perpendicular direction, the PSF exhibits a smooth, single bell-shaped profile. In contrast, the PSF along the parallel direction consists of a narrow central positive lobe flanked by two symmetric negative side lobes.

The presence of negative side lobes in the third-harmonic PSF presents a fundamental challenge for narrowband image reconstruction. PSFs with sign changes complicate deconvolution, as many deconvolution algorithms implicitly assume non-negativity. More importantly, the negative lobes introduce ambiguity in the inverse

problem: tracer located outside the intended imaging plane can partially cancel signal from in plane tracer. As a result, distinct tracer distributions may produce similar measured signals, indicating that the forward model is not strictly unique when reconstruction relies on a single harmonic.

2.4.3 Multi-Harmonic Imaging

A common reaction to narrowband imaging is thinking that useful signal is discarded by ignoring the higher harmonics of the MPI receive signal. This concern is reasonable, since those harmonics also contain information about the tracer distribution. For this reason, many MPI approaches utilize multiple harmonics for image formation rather than restricting detection to a single harmonic. However, incorporating multiple harmonics introduces additional complications in signal processing. In this section we discuss how multi-harmonic imaging is performed and outline its advantages and limitations in order to provide context for the use of narrowband detection in this work.

Utilizing multiple harmonics can in principle improve spatial resolution and image fidelity. However, each harmonic has a different PSF and therefore produces a different image of the tracer distribution, sometimes referred to as a harmonic portrait [64]. Recovering the underlying tracer distribution then requires combining these portraits through an inverse reconstruction problem.

This reconstruction is performed using linear algebra methods based on a system function that maps the tracer distribution to portrait space. The system function may be obtained through numerical simulations of the scanner or measured experimentally through calibration scans, both approaches present challenges. Accurate simulations require detailed modeling of the hardware and tracer dynamics, while experimental calibration requires extensive measurements and introduces noise. In addition, system-function reconstruction assumes that the SPIO produces the same signal during imaging as it did during calibration. If the local environment of the SPIO is different than

that of the calibration scan, the measured signal may no longer match the system function, leading to reconstruction artifacts and degraded image fidelity. As a result, system-function reconstruction lacks robustness, a common challenge when translating MPI to in-vivo imaging.

Multi-harmonic imaging also does not necessarily guarantee higher sensitivity. Although higher harmonics ($n > 3$) contain additional signal energy, their amplitudes are smaller than that of the third harmonic. For the case of white noise background, which is characteristic of MPI measurements, detection of a higher harmonic with $\text{SNR} > 1$ implies that the third harmonic is also detectable. In addition, many system-function reconstruction approaches reject harmonics with $\text{SNR} < 1$, since including high-noise channels can introduce artifacts in the reconstructed image. Consequently, incorporating additional harmonics does not necessarily improve sensitivity.

When instrument cost is considered, multi-harmonic approaches may perform worse in terms of sensitivity than narrowband systems. Narrowband detection can be implemented using a single-channel lock-in amplifier tuned to the desired harmonic. For comparable instrument cost, a lock-in amplifier can achieve substantially higher sensitivity than a general-purpose DAQ used to measure multiple harmonics.

Despite these drawbacks multi-harmonic imaging does offer several advantages. Higher harmonics have sharper PSFs, which can improve spatial resolution in the final image. In addition, the relative amplitudes of different harmonics depend on the magnetic relaxation behavior of the tracer particles. This dependence could in principle be used to probe the local environment of the tracer or enable multi-color imaging [65], [66] based on different particle states, although exploiting these effects requires accurate modeling of tracer behavior in biological environments, a non-trivial challenge in MPI.

In summary, multi-harmonic imaging can improve spatial resolution and may provide additional information about the tracer environment. However, it depends on

system-function reconstruction, which introduces modeling challenges and reduces robustness. Narrowband imaging avoids these complications by relying on a single harmonic measurement, enabling analytical image reconstruction providing robustness. In addition, narrowband systems can utilize single-channel lock-in amplifiers, reducing system cost without sacrificing sensitivity. For these reasons we believe narrowband imaging to be appropriate for our prototype system.

2.5 Image Reconstruction

This section discusses several image reconstruction techniques and their application in MPI. In MPI, the measured signal does not directly represent the spatial distribution of the SPIO. Instead, reconstruction is required to convert this signal into a meaningful image. Depending on the system, reconstruction may be essential for generating an image or used primarily to improve image quality. A variety of reconstruction methods exist, ranging from analytical approaches to numerical algorithms, each with its own strengths and limitations. The following sections will explore these methods in more detail.

2.5.1 Filtered Back Projection

For FFL based MPI systems, image reconstruction is commonly performed using the filtered back projection (FBP) method. FBP is a well-established analytical technique that has been widely used in x-ray computed tomography (CT). As the name suggests, it consists of two main steps: filtering the measured signal and back-projecting the result to form an image. As an analytical method, it offers advantages such as speed, simplicity, and robustness. It does not rely on detailed knowledge of the system response and remains stable even when the underlying physics deviate from expectations. However, because it does not account for the specific physics of MPI or the characteristics of the scanner, it can lead to artifacts or reduced spatial resolution.

2.5.1.1 Projection method To understand the FBP method it is important to first understand how an FFL scanner takes data. An FFL scanner measures the amount of SPIOs along a line segment. The line segment is then moved and the amount of SPIOs along the line segment at this new location is measured. This process is repeated for many positions of the FFL to give a function of number of SPIOs detected vs FFL position. This function is referred to as the projection of the sample. These projections can look very different depending on the angle between the FFL and the sample. An example demonstrating this is shown below.

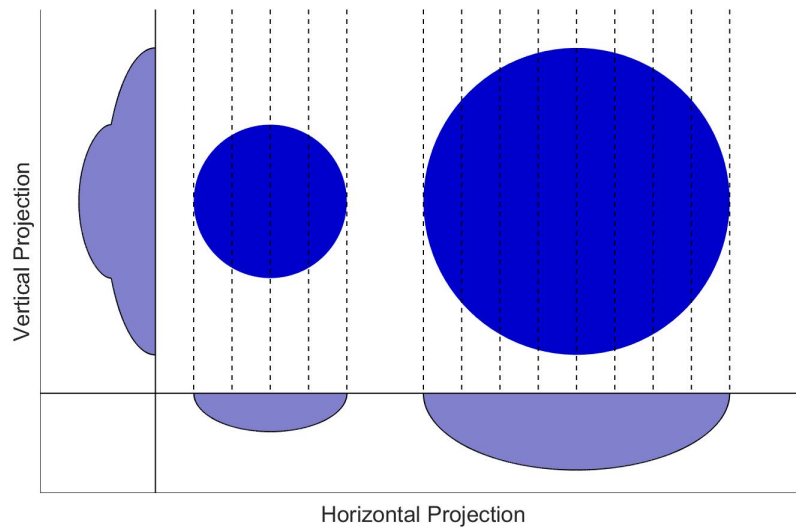


Figure 2.6: **Visualization of projection using a simple two circle phantom.** Two circles of uniform density and different sizes are projected along two different directions. Along one direction the separation between the circles can be seen while along the other direction it cannot.

The act of projection can be expressed mathematically as integration along a line segment and is sometimes referred to as the Radon transform. The Radon transform in terms of Cartesian coordinates is given by:

$$p_{\theta}(s) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} f(x,y) \delta(x \cos \theta + y \sin \theta - s) dx dy \quad (2.38)$$

where $p_{\theta}(s)$ is the projection at an angle θ , $f(x,y)$ is the sample or phantom being imaged, δ is the Dirac delta function, s is the dimension that the FFL scans across, and x and y are the Cartesian coordinates. To obtain enough information to reconstruct an image of the sample the scanner must obtain projections from an angle of 0° to an angle of 180° . Projections from 0° to 180° is referred to as a sinogram, this is because a sinogram of a point source looks like a sine wave.

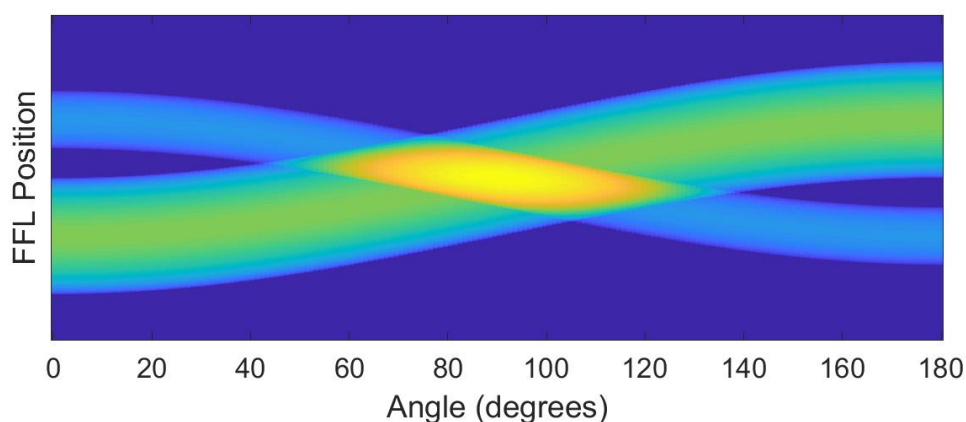


Figure 2.7: **Sinogram of a simple two circle phantom.** An image that shows how the projection of the phantom shown in Fig. 2.6 varies vs angle continuously.

2.5.1.2 Back projection Back projection as the name suggests is projection in reverse.

Note that back projection is not the inverse of projection meaning back projecting a

sinogram will not give you an image that is exactly the same as the phantom. Instead of each projection point getting the value of the line integral of the sample, like what would happen in forward projection, each point in space gets the value of the projection point that it would project on to. This means if only one projection angle is measured the corresponding back projection will simply be an that object averaged in that direction. The more projections angles used the better the reconstruction. An example displaying how the quality of a reconstructed image varies versus number of projection angles is shown below.

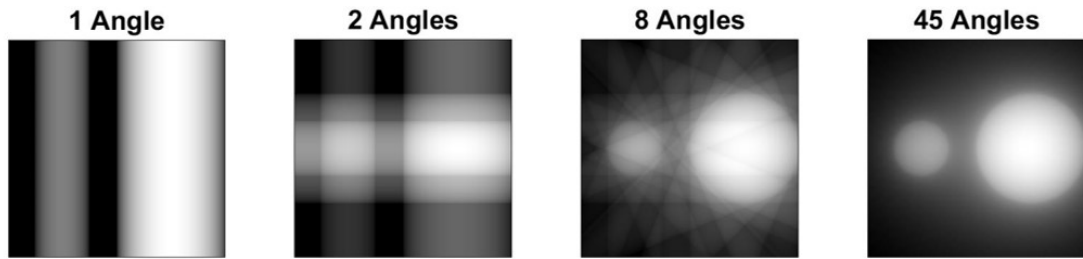


Figure 2.8: **Back projection reconstruction of a simple two circle phantom.** An image showing how the back projection reconstruction of the phantom shown in Fig. 2.6 varies versus number of projection angles. For one projection angle only the horizontal projection is measured and thus the back projected image is simply the projection smeared over the vertical direction.

The back projected image $b(x,y)$ can also be represented mathematically by a sum of the projections over all projection angles. This takes the form of the following integral:

$$b(x,y) = \int_{0^{\circ}}^{180^{\circ}} p(\theta, s = x\cos\theta + y\sin\theta) d\theta \quad (2.39)$$

2.5.1.3 Filtering Back projection by itself is a good tool for reconstructing an image from a sinogram, but it isn't perfect. The main issue with back projected images is the soft glow that can be seen on edges of objects, this effect can be seen in Fig. 2.8. This effect can best be understood in Fourier domain. When performing a scan of an object the scanner over samples the low frequency components of the object and under samples its high frequency components. The high frequency components are responsible for sharp features in the image such as edges so an under sampling of them would lead to smoother edges. In order to correct this mistake filtering is done in Fourier space by multiplying by a filter function $H(\omega)$. The filter which makes back projection the true inverse of forward projection is the ramp filter $H_{\text{ramp}}(\omega)$ and is given by:

$$H_{\text{ramp}}(\omega) = |\omega| \quad (2.40)$$

where ω is the spatial frequency. This filter gets its name from the shape it makes.

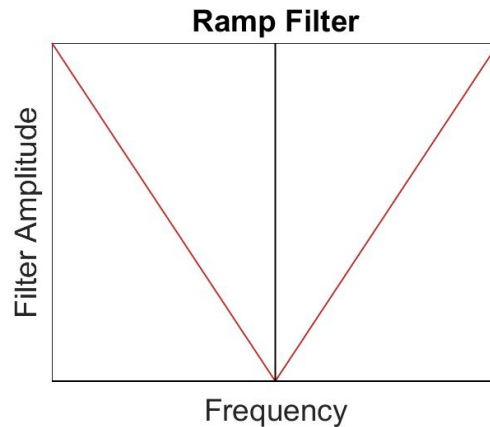


Figure 2.9: **Ramp filter amplitude versus frequency.** The ramp filter makes filtered back projection a true inverse of the forward projection.

Despite the ramp filter being the only filter that makes the FBP method a true inverse of projection it is rarely used in MPI. This is because in practice the ramp filter amplifies noise. The ramp filter amplifies noise because noise has very high spatial frequency, and the ramp filter amplifies high frequencies. To solve this issue there are many filters that multiply the ramp filter by another function to suppress the high frequencies. The simplest of such filters is the Ram-Lak filter which multiplies the ramp filter by a rectangle function essentially cutting off all frequencies above a certain threshold. The mathematical expression for the Ram-Lak filter is:

$$H_{\text{Ram-Lak}}(\omega) = |\omega| \cdot \Pi(\omega/L) \quad (2.41)$$

where $\Pi()$ is the rectangle function, and L is an adjustable parameter that sets the cutoff frequency. The Ram-Lak filter solves the issue of amplifying high frequency noise but it is discontinuous at the cutoff frequency. Other filters try and solve this issue by multiplying by a continuous function. Examples of such filters include the Shepp-Logan filter, the Cosine filter, and the Hann filter. The mathematical expression of such filters is as follows:

$$H_{\text{Shepp-Logan}}(\omega) = |\omega| \cdot \text{sinc}\left(\frac{\omega}{2}\right) \quad (2.42)$$

$$H_{\text{Cosine}}(\omega) = |\omega| \cdot \cos\left(\frac{\omega}{2}\right) \quad (2.43)$$

$$H_{\text{Hann}}(\omega) = |\omega| \cdot \left(0.5 + 0.5\cos\left(\frac{\omega}{2}\right)\right) \quad (2.44)$$

where $\text{sinc}()$ and $\cos()$ have there standard definitions. A graph comparing the shapes of these different filters in shown below.

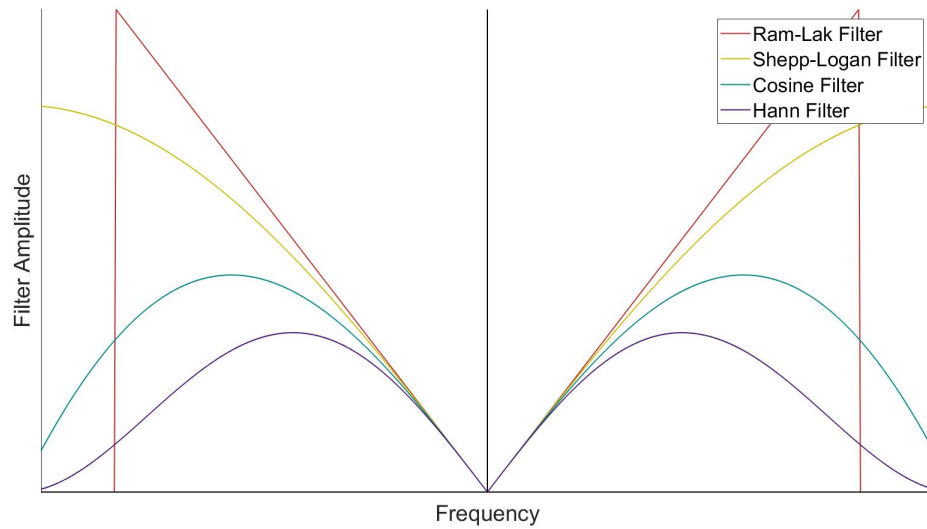


Figure 2.10: **Comparison between Ram-Lak, Shepp-Logan, Cosine, and Hann filters.**

The Ram-Lak filter is the closest to the ramp filter so it's best used when you have a phantom whose features can be easily separated from the noise in Fourier space. The Hann filter has the fastest drop off of any of the filters, and thus is the best at reducing noise. The Shepp-Logan and Cosine filters are in between cases that may give the best image quality depending on the situation.

2.5.2 Iterative Reconstruction

Iterative reconstruction methods, also known as system function approaches, treat MPI reconstruction as a linear inverse problem, analogous to those used in modalities such as PET and CT. The desired image is represented as a vector $\mathbf{x}$ containing the spatial distribution of tracer concentration, while the measurement data are collected in a vector $\mathbf{p}$. In our work this signal space corresponds to the measured third-harmonic amplitudes at different FFL positions, but more generally $\mathbf{p}$ can be considered the detector space of the

scanner. The forward model is expressed as

$$\mathbf{p} = \mathbf{A}\mathbf{x}, \quad (2.45)$$

where $\mathbf{A}$ is the system matrix describing the mapping from image space to measurement space, incorporating the physics of the scanner such as coil geometries, FFL trajectory, and the nonlinear tracer response.

In principle, if $\mathbf{A}$ were exactly known and invertible, the image could be obtained directly by

$$\mathbf{x} = \mathbf{A}^{-1}\mathbf{p}. \quad (2.46)$$

In practice, however, $\mathbf{A}$ is large, ill-conditioned, and the measured data $\mathbf{p}$ are corrupted by noise. Direct inversion is therefore unstable, and iterative algorithms are instead employed. These methods begin with an initial guess $\mathbf{x}_0$ and refine it through successive updates using forward and backward operations. A common update rule is

$$\mathbf{x}_{k+1} = \mathbf{x}_k + \alpha \mathbf{A}^T (\mathbf{p} - \mathbf{A}\mathbf{x}_k), \quad (2.47)$$

where α is a relaxation parameter. This scheme, known as Landweber iteration, is closely related to gradient descent and provides the conceptual foundation for more advanced algorithms. Iterations may be terminated when a stopping criterion is reached, or tuned manually to yield the best image quality.

The advantage of iterative reconstruction is that it can fully exploit the physics of the system to recover the tracer distribution. This allows for improved resolution and sensitivity, and inherently performs deconvolution. Iterative methods can also combine information from multiple signal channels: for example, rather than reconstructing an image separately from each harmonic, data from all harmonics can be incorporated into a single reconstruction, boosting both SNR and resolution.

Despite these strengths, iterative methods have important drawbacks. They are computationally intensive, with reconstructions often requiring tens of minutes, making them impractical for real-time imaging. They also suffer from poorly defined stopping conditions, particularly in MPI, which requires manual tuning of the number of iterations and thus expert supervision. Most critically, iterative methods rely heavily on an accurate system function $\mathbf{A}$. Discrepancies between the modeled or measured system function and the true system lead to artifacts in the reconstructed images. Simulating $\mathbf{A}$ is difficult, as it requires capturing all physical effects and imperfections of the scanner. As a result, many groups measure $\mathbf{A}$ empirically by scanning a point tracer across the FOV. This procedure is time consuming (often requiring days) and introduces noise into the system matrix, which in turn propagates into the reconstructed image. Moreover, there is no guarantee that tracer behavior measured in calibration phantoms will match tracer behavior in vivo, so system functions derived from calibration may accurately reconstruct tracer located in a biological environment.

In summary, system function approaches are promising because they can improve sensitivity, resolution, and artifact suppression by explicitly modeling the imaging process. However, they are challenging to implement in practice, computationally demanding, sensitive to errors in the system function, and lack robustness across varying imaging conditions. For these reasons, we have not yet implemented iterative reconstruction in our scanner, though it remains a promising technique to explore in the future.

2.5.2.1 Understanding the System Function A natural question when first encountering system-function approaches is what exactly the system function $\mathbf{A}$ represents and how it is obtained. To gain insight, it is helpful to write out the matrix multiplication explicitly:

$$\begin{bmatrix} p_1 \\ p_2 \\ \vdots \\ p_m \end{bmatrix} = \begin{bmatrix} a_{1,1} & a_{1,2} & \dots & a_{1,n} \\ a_{2,1} & a_{2,2} & \dots & a_{2,n} \\ \vdots & \vdots & \vdots & \vdots \\ a_{m,1} & a_{m,2} & \dots & a_{m,n} \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ \vdots \\ x_n \end{bmatrix}.$$

Here $\mathbf{p} \in \mathbb{R}^m$ is the vector of measured signals, with m entries corresponding to different FFL positions (or more generally, measurement channels). The vector $\mathbf{x} \in \mathbb{R}^n$ represents the tracer concentration at n discrete spatial locations. The system matrix $\mathbf{A}$ has dimensions $m \times n$, where each entry $a_{i,j}$ describes the contribution to measurement p_i from a unit concentration of tracer located at voxel j .

Equivalently, each row of $\mathbf{A}$ can be interpreted as the system's response to a point source placed at a specific spatial location. Measuring or simulating the response of the scanner to such a point source provides the coefficients $a_{i,j}$, which collectively form the system matrix. In MPI, this point source response corresponds to the effective point spread function sampled at the i -th measurement position.

In practice, $\mathbf{A}$ can be obtained in two ways. One approach is to simulate the scanner physics, including coil geometries, field profiles, and tracer magnetization dynamics. This provides a noise free system function but requires accurate modeling of all hardware and particle behavior. The alternative is to measure $\mathbf{A}$ empirically by scanning a small tracer sample (a “delta sample” or calibration phantom) across the FOV and recording the measured signals. While this captures the real system response including imperfections, it is time consuming and introduces calibration noise. Regardless of the method, the system function embodies the full mapping from tracer concentration to measured signal and determines the success of iterative reconstruction.

2.5.3 Machine Learning Reconstruction

Machine learning methods have recently emerged as powerful tools for image reconstruction across many modalities, including MPI. In this context, machine learning can be viewed as a data driven alternative to explicit system function approaches. Instead of modeling the physics of the scanner through a system matrix $\mathbf{A}$, a neural network is trained to learn the mapping from measurement space to image space directly.

Neural networks are typically trained in a supervised manner: given pairs of input signals (e.g., harmonic amplitudes at various FFL positions) and target images (tracer distributions), the network parameters are optimized using gradient descent to minimize the reconstruction error. Once trained, the network effectively acts as an implicit system function that replaces $\mathbf{A}$ and its inversion. Training data can be generated either from forward simulations of MPI physics or obtained from large experimental datasets. In practice, many groups rely on simulated data due to the difficulty of collecting sufficiently large experimental datasets, although combining both sources can improve robustness.

A popular architecture for MPI reconstruction is the U-Net, a convolutional neural network originally developed for biomedical image segmentation. U-Nets and similar encoder-decoder architectures are well suited to MPI because they can capture spatial features and generalize them to higher order latent space information. Other approaches include fully connected networks for low-dimensional problems and generative adversarial networks (GANs) for enhancing image quality.

Machine learning reconstruction offers several potential advantages. Reconstruction is extremely fast once the network is trained, making real time imaging feasible. Neural networks can also incorporate learned priors that suppress noise and artifacts, often producing images that appear sharper and cleaner than conventional reconstructions. Furthermore, ML methods can implicitly combine multi-harmonic information without requiring explicit calibration or matrix inversion.

However, these benefits come with significant challenges. Training requires large, diverse datasets which are difficult to obtain in MPI. Networks trained on simulated data may not generalize well to the real scanner, and networks in general may not generalize to in-vivo measurements if the tracer properties or system response differ from the training conditions. Unlike linear reconstruction methods, neural networks are often treated as “black boxes,” making it difficult to interpret how the reconstructed image relates to the measured data. Finally, retraining is required if scanner hardware or tracer properties change substantially, which can limit robustness in practical applications.

Overall, machine learning represents a promising but still experimental approach for MPI reconstruction. It offers speed and robustness once trained, but its reliance on training data and limited interpretability remain significant barriers compared to more established system function methods.

2.6 Tracer Particles

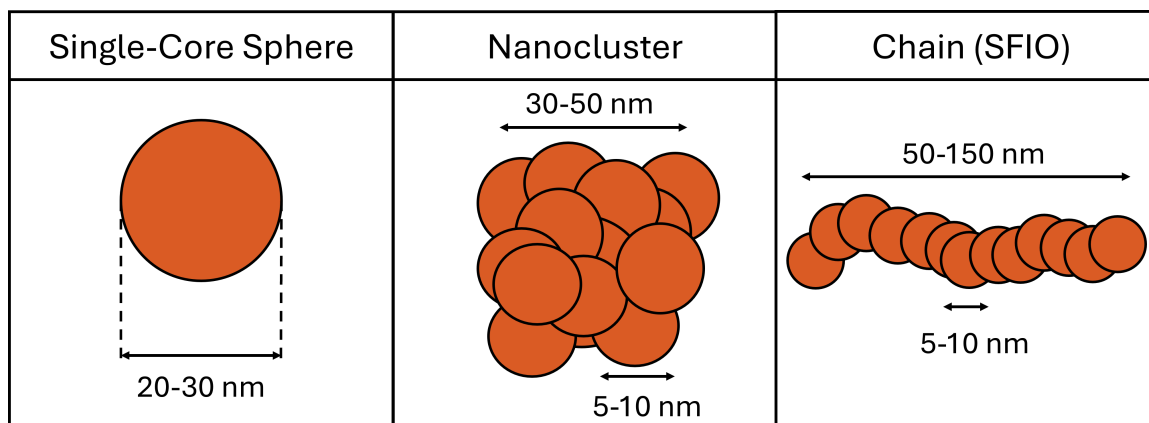


Figure 2.11: **Representative geometries and dimensions of MPI tracer particles.** Schematic comparison of various SPIO tracer geometries used in MPI. Left: Single-core spherical particles with magnetic core diameters of 20-30 nm. Center: Cluster particles composed of clustered crystallites (5-10 nm) forming aggregates with overall diameters of 30-50 nm. Right: Chain or superferromagnetic iron oxide (SFIO) particles consisting of 5-10 nm cores arranged into chains with characteristic lengths of 50-150 nm. Dimensions shown refer to magnetic core sizes; hydrodynamic diameters may be larger.

As a tracer-based imaging modality, the viability and performance of MPI depend strongly on the magnetic tracer particles themselves. Access to suitable tracers is a prerequisite for imaging, and improvements in tracer performance would relax hardware constraints, potentially facilitating clinical translation. As a result, tracer development has become a rich and active area of research within MPI, with entire dissertations focused on the study of particle design, synthesis, and characterization.

While the primary focus of this dissertation is the development of single-sided MPI hardware, the central role of SPIO tracers in determining sensitivity, spatial

resolution, and overall imaging performance necessitates some discussion of their behavior. This section therefore aims to provide a brief overview of MPI tracer particles, including the physical principles governing their response, the current standard tracers used in the field, and future directions in tracer development. Ultimately, successful clinical translation of MPI will likely require coordinated advances in both hardware and tracer technology, making an understanding of tracer performance important for interpreting the results presented in this work.

2.6.1 Ideal Tracer Qualities

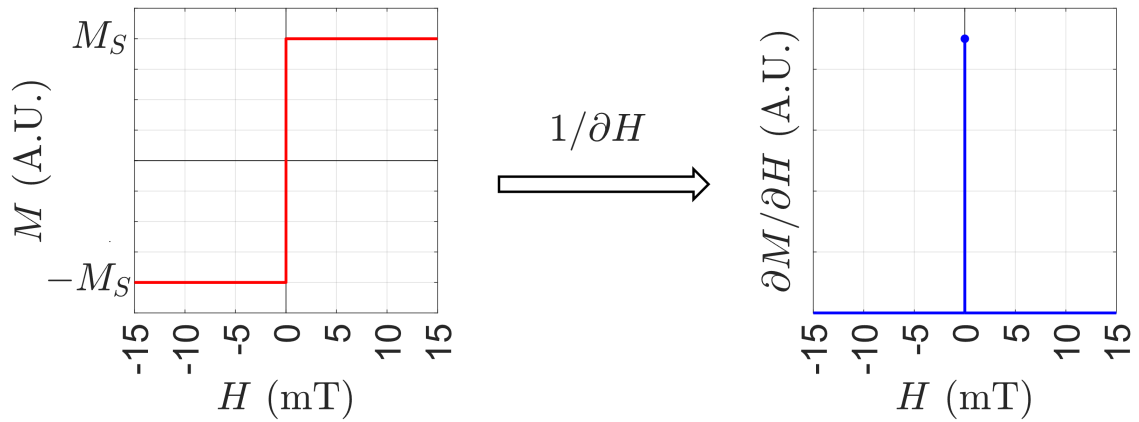


Figure 2.12: **Magnetization curve of ideal MPI tracer particles.** Idealized magnetization curve $M(H)$ for a theoretical MPI tracer particle shown as a step function with saturation at $\pm M_S$, and its corresponding derivative $\partial M / \partial H$ shown as a sharply localized peak centered at zero field.

To understand what makes a tracer desirable in MPI, it is useful to consider a theoretical ideal particle. An ideal MPI tracer would exhibit a strong magnetic response (high susceptibility χ) while having no remanent magnetization or hysteresis. In practical

terms, this means that the application of a magnetic field H induces a net magnetization M , and that this magnetization depends only on the instantaneous applied field, not on its previous state.

A highly magnetic tracer is one whose magnetization rapidly approaches the saturation magnetization M_S under relatively small applied fields. The saturation magnetization (M_S) corresponds to the state in which the magnetic moments of all particles in the ensemble are aligned. While the terms "highly magnetic" and "low field" are relative, in practice this typically implies that saturation is reached at field strengths on the order of ~ 20 mT. In the theoretical limit, an ideal tracer would reach M_S under arbitrarily small applied fields. In this case, the magnetization curve would approach a step function, as illustrated in Fig. 2.12.

The desirability of such a magnetization curve becomes clear when considering the derivative $\partial M / \partial H$. For an ideal step $M(H)$ curve, this derivative would take the form of a sharply localized peak centered at zero field. As shown in Eq. 2.9, the induced receive signal in MPI is proportional to the time derivative of the magnetization, which in turn depends on the slope of the magnetization curve with respect to the applied field. A steeper $M(H)$ transition therefore produces a larger signal amplitude for a given excitation field.

In addition to maximizing signal, the derivative $\partial M / \partial H$ determines the PSF in MPI (see Eq. 2.14). As explained in Sec. 2.4.2, the ideal PSF is a delta function because this yields a one-to-one mapping between spatial position and measured signal. The width of the PSF, together with the gradient strength, determines the spatial resolution of the scanner, $x_{\text{res}} = \text{FWHM} / G$, so a sharper peak leads to improved resolution. The step function therefore represents the optimal $M(H)$ curve.

The absence of remanent magnetization and hysteresis is equally important. If a tracer exhibits hysteresis, the magnetization for a given applied field depends on whether

the field is increasing or decreasing. In MPI, hysteresis leads to different magnetization responses during different portions of the excitation cycle even when the FFR is positioned at the same spatial location. As a result, the measured signal effectively represents a superposition of two history-dependent responses, which complicates signal interpretation and image reconstruction. For these reasons, MPI tracers are ideally superparamagnetic, exhibiting negligible coercivity and remanence, so that their magnetization is single-valued and reversible with respect to the applied field.

2.6.2 Classical Single-Core Sphere

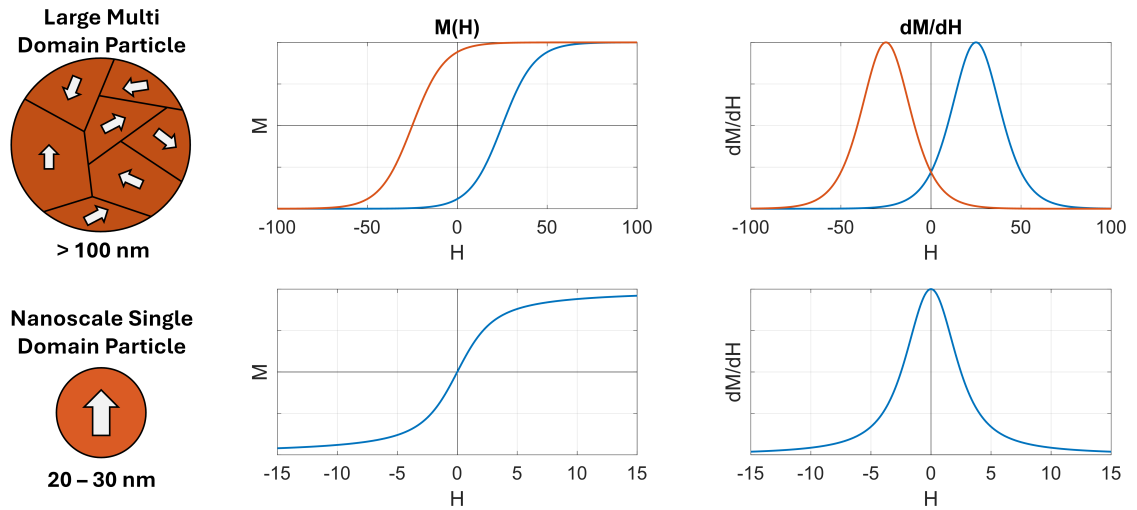


Figure 2.13: **Single-core spherical tracer particles.** Schematic illustration of a multi-domain ferrimagnetic particle and a single-domain superparamagnetic particle, along with representative magnetization curves $M(H)$ and their corresponding derivatives $\partial M/\partial H$.

The current and historically dominant tracer material used in MPI is magnetite (Fe_3O_4). At first glance, this choice appears counterintuitive, since bulk magnetite is a

ferrimagnetic material. In bulk form, magnetite consists of multiple magnetic domains whose moments partially cancel, resulting in a reduced effective susceptibility and a magnetization response that depends on magnetic history. This multi-domain structure leads to nonzero coercivity and remanence, which is undesirable for MPI.

To obtain the magnetic behavior required for MPI, magnetite must be fabricated as sufficiently small particles such that only a single magnetic domain exists within each particle. When the particle diameter is reduced below a critical size, typically on the order of 20-30 nm, the formation of multiple domains becomes energetically unfavorable. In this regime magnetite exhibits superparamagnetism, featuring strong susceptibility and negligible coercivity and remanence. Compared to bulk ferrimagnetic material, this results in a much steeper $M(H)$ curve near zero field and a correspondingly sharper $\partial M/\partial H$ response, as illustrated in Fig. 2.13. These properties make single-core spherical SPIOs well suited for MPI, providing strong signal amplitude and improved spatial resolution relative to multi-domain particles.

Historically, the monodisperse single-core spherical SPIO was considered the theoretically optimal tracer particle for MPI. Early work focused on identifying the largest particle size that would remain single-domain, as well as developing reliable synthesis methods to produce particles with narrow size distributions. Numerous research groups produced custom magnetite tracers optimized for MPI performance based on this design principle.

A commercially available example of this tracer class is Vivotrax, which has become a widely used standard in MPI research. Although not perfectly monodisperse or optimized relative to theoretical limits, Vivotrax represents a practical implementation of the single-core spherical SPIO concept and has been used extensively for system characterization, phantom imaging, and early biological studies.

2.6.3 Cluster Particles

While early MPI tracer development focused on single-core spherical particles, subsequent work demonstrated that more complex nanoparticle geometries can provide substantially improved imaging performance. In particular, multicore or cluster SPIO tracers have become dominant in modern MPI studies due to their superior magnetic properties, leading to improved sensitivity and spatial resolution [67], [68].

Cluster particles consist of many nanocrystalline iron oxide cores, typically 5–10 nm in diameter, each forming a single magnetic domain, which are agglomerated into a larger composite particle with a characteristic size of approximately 50–70 nm (see Fig. 2.11). Compared to single-core particles of equivalent iron mass, these cluster tracers exhibit a larger effective magnetic moment, increased susceptibility, and a steeper magnetization slope near zero field. These properties directly lead to increased signal magnitude and improved spatial resolution [69], [70].

The physical origin of this enhanced performance is nontrivial and does not admit a simple analytical description. Magnetic interactions among the closely packed crystallites within a cluster involve dipolar coupling, collective magnetization dynamics, and anisotropy effects. As a result, accurate modeling of cluster behavior typically requires micromagnetic or Monte Carlo simulations [71]. Despite the absence of a complete theoretical framework, the empirical benefits of cluster tracers for MPI are well established. Experimental studies have consistently shown increases in signal intensity and narrower PSFs relative to single-core spherical tracers of equal iron mass [72], [73].

Among cluster tracers, nanoflower particles have emerged as particularly effective for MPI. Nanoflowers are a subclass of cluster particles in which the crystallites are arranged dendritic structure with sharp branched "petals", giving them the name nanoflower. This structure gives them a significantly higher surface-to-volume ratio than traditional spherical SPIO. They exhibit strong superparamagnetism (no magnetic

memory) and high magnetic moments per particle. Two nanoflower tracers that are widely used in MPI research are Perimag and Synomag-D [73]. These tracers have become de facto standards for experimental MPI due to their high sensitivity and favorable spatial resolution performance.

2.6.4 Superferromagnetic Particles

A recent and promising direction in MPI tracer development is the use of superferromagnetic iron oxide nanoparticles (SFIO). As the name suggests, SFIO behave ferromagnetically rather than superparamagnetically, meaning that magnetic hysteresis is present. SFIO consist of multiple small single-core iron oxide particles (typically ~ 5 nm in diameter) that assemble into elongated chain like geometries with lengths on the order of 50-150 nm. These chain SFIO are desirable because they demonstrate order-of-magnitude gains in both sensitivity and spatial resolution compared with standard tracers under otherwise similar scanner conditions [74], [75].

Chain particles are not solely a synthetic, but also occur naturally as magnetosome chains produced by magnetotactic bacteria. These organisms biosynthesize membrane-bound magnetite crystals and organize them into linear chains for magnetic navigation. MPI imaging of these naturally occurring magnetosome chains has been demonstrated [76], highlighting the potential of this particle geometry and suggesting a possible pathway toward biocompatible tracer designs.

Although chain particles show immense potential through their order-of-magnitude improvements in sensitivity and spatial resolution, they also introduce significant challenges that currently limit their adoption. First, the hysteresis exhibited by SFIO complicates image formation. Standard MPI hardware and imaging strategies are designed for superparamagnetic tracers with no hysteresis, and applying these approaches directly to hysteretic tracers results in non-trivial artifacts in the reconstructed images. Alternative imaging strategies have been explored to accommodate the hysteretic response

of SFIO, but these methods are non-trivial to implement and require specialized hardware and tailored acquisition and reconstruction strategies [77].

Second, the long-chain morphology of these particles raises translational concerns for in vivo use. Chain particles exhibit larger hydrodynamic sizes and more complex clearance behavior than conventional single-core or cluster SPIO formulations. While bacterial magnetosomes are actively studied for biomedical applications, their in vivo toxicity, and clearance require systematic validation and may depend strongly on surface modification and formulation. Finally, because hysteresis loops dissipate energy, hysteretic tracers may increase the potential for tissue heating under alternating magnetic fields. In MPI, heat generation is linked to hysteresis losses, motivating additional safety and sequence design considerations when using SFIO tracers [78].

CHAPTER THREE

SIMULATIONS

To effectively design and improve our MPI scanner, physics based simulations were needed for rapid prototyping and development. Because MPI is a relatively new field, and because both the topology of our scanner and its scanning methodology are unique, no existing simulation tools were available that could be directly applied to our system. As a result, a substantial portion of this dissertation work was devoted to developing custom software tools capable of modeling the electromagnetic fields produced by the scanner, and the imaging process. These simulations supported hardware prototyping and enabled the refinement of scanning protocols. Additionally, they supported the exploration of advanced image reconstruction strategies. This chapter describes the simulations developed, the theoretical principles on which they are based, and representative results that illustrate their capabilities.

3.1 Electromagnetic Coil Simulations

The topology and hardware of an MPI scanner are determined by the number and geometry of its electromagnetic coils. As such, modeling the coils is necessary for modeling the scanner. The coil geometry determines the magnetic field profiles and the field strength per unit current, which in turn determine the scanner's sensitivity, spatial resolution, and FFL formation and scanning behavior.

To model the electromagnetic coils, a Biot–Savart numerical simulation was developed in MATLAB¹. This script enables simulation of arbitrary coil geometries, including racetrack-shaped coils, circular coils, and other complex configurations. The user defines the coil geometry, and the simulation calculates the magnetic field vector at user-specified positions in space. This tool was used for rapid prototyping of new coil

¹The MATLAB implementation of the Biot–Savart simulation is provided in Appendix B.1.

geometries for both receive and excitation coils, as well as for modeling the selection coils responsible for FFL generation and control.

3.1.1 Numerical Method

The magnetic fields were simulated in MATLAB using a numerical approximation of the Biot–Savart law. This approach enables calculation of the magnetic field generated by arbitrary coil geometries. The resulting field maps can be used for direct comparison with measured data or as input for more advanced simulations discussed later in this chapter.

The Biot–Savart law defines the magnetic field $\vec{B}$ produced by a current-carrying conductor as

$$\vec{B} = \frac{\mu_0 I}{4\pi} \int \frac{d\vec{l} \times (\vec{r} - \vec{r}')}{|\vec{r} - \vec{r}'|^3} \approx \frac{\mu_0 I}{4\pi} \sum_{\text{coil}} \frac{d\vec{l} \times (\vec{r} - \vec{r}')}{|\vec{r} - \vec{r}'|^3}, \quad (3.1)$$

where $d\vec{l}$ is an infinitesimal segment of the current-carrying wire, $\vec{r}$ is the position at which the field is evaluated, and $\vec{r}'$ is the position of the wire element. The integral is replaced by a discrete summation over all wire segments defining the coil geometry.

This implementation assumes a thin-wire approximation, where each conductor is treated as an infinitesimal current path with no cross-sectional area. As a result, the simulation does not account for effects such as current distribution or proximity fields within thick or multi-turn conductors. Despite this limitation, the thin-wire model provides an accurate estimate of the magnetic field in the regions of interest relevant to scanner design.

By evaluating the field at multiple spatial locations $\vec{r}$, the user can compute the magnetic field over an arbitrary volume or plane. All fields are calculated at unit current ($I = 1$ A) and scaled linearly to the desired operating current. The calculated field

components are saved for later use in other simulation scripts or for comparison with measured magnetic field data.

3.1.2 Selection Coil Simulations

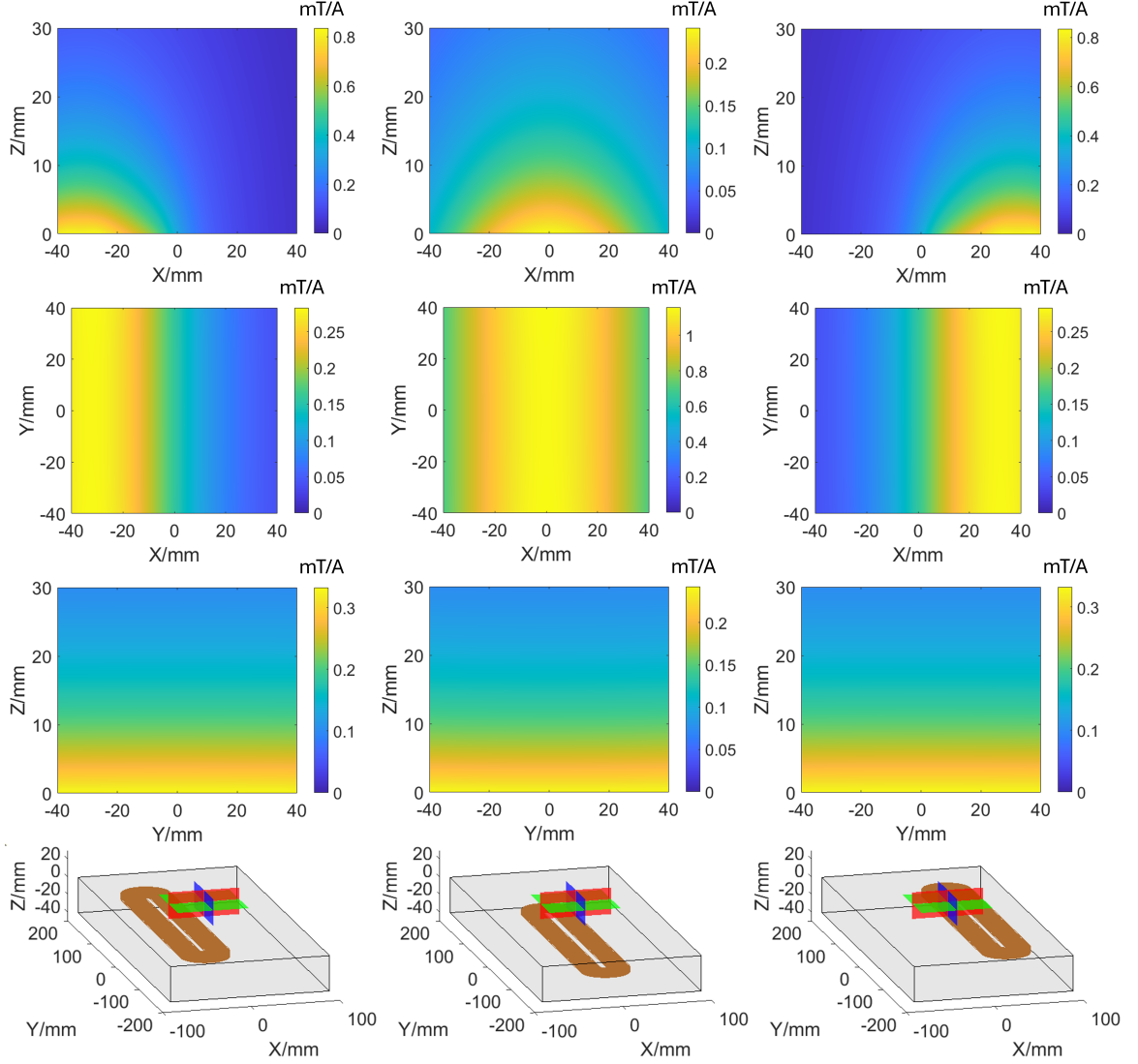


Figure 3.1: **Simulated Selection Coils.** Magnetic field simulations of the three racetrack-shaped selection coils in the XY (green), XZ (red), and YZ (blue) planes, shown in the first three rows. The bottom row shows the 3D geometry of the coils and the orientation of each simulated plane. Color maps represent the magnetic field magnitude normalized per ampere of current ($|B|/A$).

The primary coils that make up our unique hardware are the three internal racetrack-shaped coils. The coils have a racetrack length of 305 mm and a width of 55 mm. Two of the coils are located 7 mm below the surface of the scanner and are separated by 64 mm (center-to-center), positioned symmetrically about the scanner's center. These two coils are referred to as the selection coils, as they are responsible for spatial encoding because they form and scan the FFL. Therefore, modeling of these coils allows us to determine how to form and scan the FFL and to estimate achievable spatial resolutions. The third racetrack-shaped coil is located in the center of the scanner, 24 mm below the surface. Depending on the scanner implementation, this coil either acts as an excitation coil supplying an AC magnetic field to the SPIO sample or as an auxiliary selection coil, allowing for greater control of the FFL position. Modeling this coil allows us to estimate the possible sensitivity of our scanner or model how to fully control and scan our FFL.

All three coils were simulated individually using the Biot–Savart field calculator described previously. The magnetic field was computed in three orthogonal planes: the XZ plane² (red plane in Fig. 3.1), the XY plane (green plane), and the YZ plane (blue plane). Each coil was simulated with a unit current ($I = 1$ A), and field magnitudes are therefore reported in mT/A. The resulting plots (Fig. 3.1) show the magnitude of the total magnetic field $|\vec{B}|$ across each plane.

The simulations show that, due to the elongated geometry of the coils along the y-axis, the magnetic fields are homogeneous in that direction. The strongest field gradients occur near the scanner surface and weaken with increasing z . Consequently, higher operating currents are required at larger imaging heights to achieve the same gradient strength (which determines spatial resolution) and excitation amplitude (which determines sensitivity).

²The coordinate system of the scanner is shown in Fig. 1.5(b,d) and in the bottom row of Fig. 3.1.

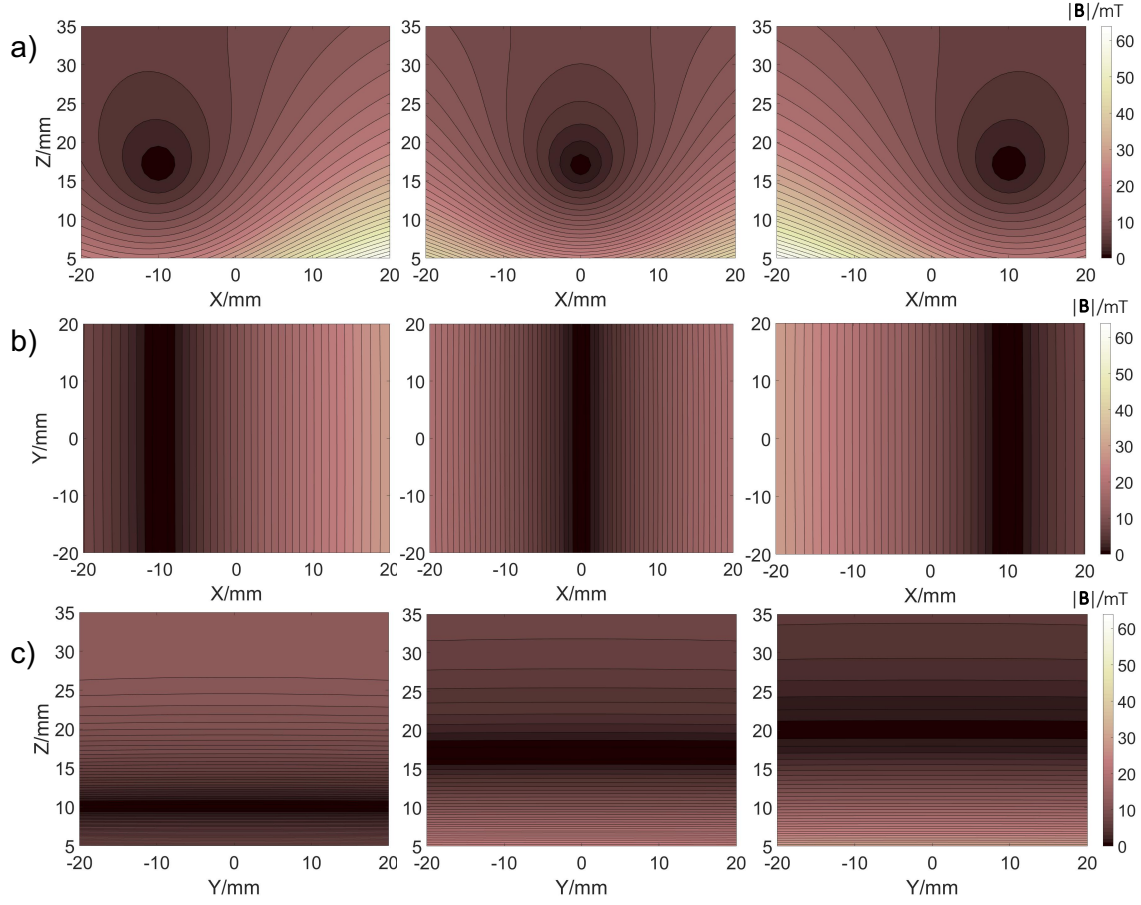


Figure 3.2: **Simulated FFL Generation.** Simulated magnetic field contour plots $|\mathbf{B}|/\text{mT}$. Rows: a) XZ and b) XY planes showing FFL translations along x-axis with a linear corrected trajectory at the height $z=17$ mm. c) YZ plane showing FFL at $x=0$ and various slices $z=10$ mm, $z=17$ mm, $z=20$ mm.

3.1.2.1 FFL Formation and Scanning From the simulated selection fields we can simulate FFL formation and control. The total selection field is given as a superposition of the individual selection fields:

$$B_{\text{sel}} = I_1 P_1 + I_2 P_2 + I_3 P_3, \quad (3.2)$$

where I_i is the current in selection coil i , and P_i is the magnetic field produced by selection coil i per unit current. In the case where $I_3 = 0$ and $I_1 = I_2$, the two opposing magnetic fields cancel along the central axis ($x = 0$ mm), forming a field-free line (FFL) at a height of $z = 17$ mm above the scanner surface, as shown in Fig. 3.2 (center column).

Varying the ratio of the selection coil currents allows the FFL to be translated laterally in the x -direction across the field of view, enabling spatial encoding. For example, increasing I_1 relative to I_2 shifts the FFL toward positive x positions, while increasing I_2 shifts it toward negative x positions. This controllable translation forms the basis of the discrete stepping imaging method used in our scanner. The simulated magnetic field maps shown in Fig. 3.2 illustrate these cases, where each column corresponds to a different FFL position achieved by adjusting the relative selection coil currents.

3.1.3 Receive Coil Simulation

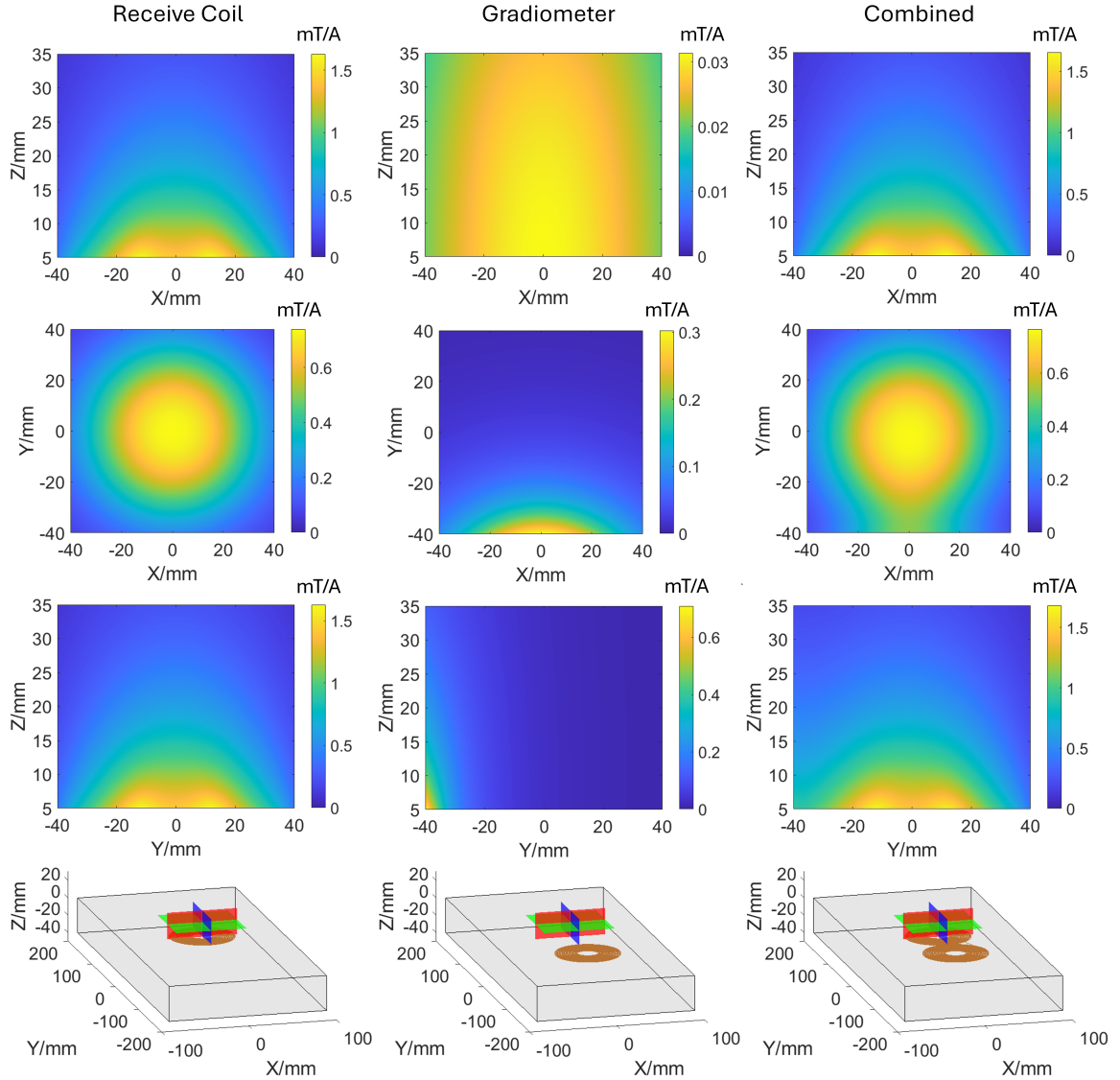


Figure 3.3: **Simulated Receive Coil.** Magnetic field simulations of the surface receive and gradiometer coils in the XY (green), XZ (red), and YZ (blue) planes, shown in the first three rows. The bottom row shows the 3D geometry of the coils and the orientation of each simulated plane. Color maps represent the magnetic field magnitude normalized per ampere of current ($|\mathbf{B}|/\text{A}$).

In addition to the excitation coil, the overall sensitivity of the scanner is determined by the receive coil. The receive coil is positioned near the imaging region to detect the oscillating magnetization of the SPIO sample as an induced voltage through Faraday induction. According to the reciprocity principle, this induced voltage is proportional to the magnetic field that would be produced by the same coil carrying a unit current at the location of the SPIO sample. Therefore, simulating the magnetic field generated by the receive coil provides a direct measure of its spatial sensitivity profile. Uniformity of this field distribution determines how evenly the scanner detects signal across the FOV, with nonuniform sensitivity leading to intensity variations in reconstructed images.

Our single-sided scanner supports modular surface receive coils, several of which have been proposed and experimentally demonstrated in previous work [79]. The design utilized for imaging in this work consists of a circular receive coil paired with an identical, laterally displaced coil functioning as a gradiometer. The primary receive coil has an inner diameter of 25 mm, an outer diameter of 60 mm, and a total of 38 turns arranged in a dual-layer configuration. It was designed for optimal uniformity of the sensitivity profile approximately 10 mm above the coil center. The second coil, identical in geometry, is positioned 70 mm away along the y-axis and wired in opposition to form the gradiometer pair. The purpose of this configuration is to suppress common-mode background signal, feedthrough from the excitation coil. Because the gradiometer is sufficiently distant from the FOV, it minimally distorts the sensitivity pattern of the primary receive coil (see Fig. 3.3).

The simulated magnetic fields of both the receive and gradiometer coils are shown in Fig. 3.3. The receive coil exhibits lateral uniformity in the XY plane across a 4 cm FOV, providing homogeneous detection sensitivity over this region. However, sensitivity decreases toward the periphery at an 8 cm FOV, leading to less uniform images over larger FOVs. The gradiometer coil has negligible effect on the overall uniformity of the receive

coil's field, confirming that the spatial separation between the coils is sufficient to maintain consistent sensitivity within the imaging volume while canceling background feedthrough.

3.1.4 Surface-Volume Excitation Coil Simulations

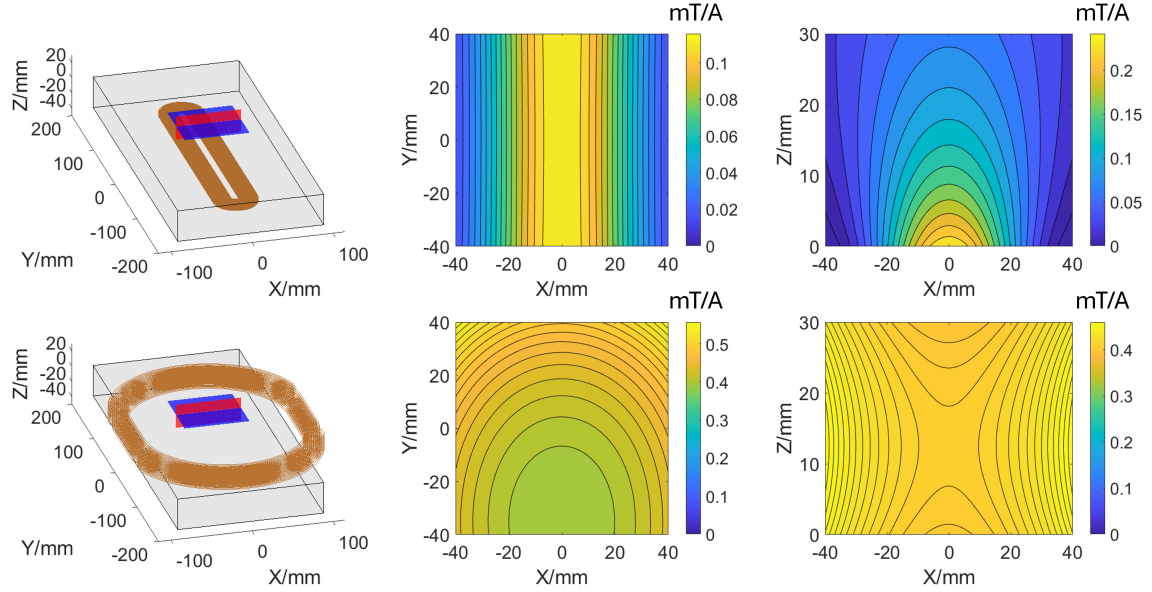


Figure 3.4: **Simulated Surface-Volume Excitation Coil.** Magnetic field simulations comparing the original excitation coil (top row) and the new surface excitation coil (bottom row). The first column shows the geometry and placement of each coil on the scanner, with the blue plane indicating the XY plane and the red plane indicating the XZ plane where the fields were simulated. The second column shows the simulated z-component of the magnetic field (B_z) in the XY plane, and the third column shows the corresponding B_z field in the XZ plane. Color maps are normalized per ampere of applied current. The new surface excitation coil demonstrates improved excitation field strength and homogeneity compared to the original embedded coil.

A major limitation of the original implementation of our scanner was low sensitivity, a challenge common to all single-sided MPI systems [42], [55], [56]. To address this limitation, we designed and developed a surface-volume excitation coil, a

paradigm-shifting coil topology for single-sided scanners. The surface–volume coil is designed to surround the imaging FOV, providing superior excitation field strength and homogeneity across the imaging region.

The excitation coil is configured to accommodate and partially enclose a specific body region for a targeted application, such as breast cancer diagnostics. For other anatomies, application specific coils can be designed and interchanged due to their surface-mounted configuration, making them modular. The current implementation of this coil features a racetrack geometry with an inner bend diameter of 195 mm and a straight segment length of 70 mm along the long axis, providing clearance for the subject table and imposing no additional constraints on maximum subject size. The overall outer dimensions are 315 mm in length, 245 mm in width, and 28.5 mm in height. The coil consists of eight layers with ten turns per layer.

The magnetic fields produced by the surface excitation coil were simulated using the Biot–Savart field calculator. Fig. 3.4 compares the simulated magnetic fields of the original and new excitation coils. The XY-plane fields (center column) show that the surface excitation coil achieves improved uniformity across an 8 cm FOV, along with higher field strength compared to the original embedded excitation coil. The XZ-plane fields (right column) demonstrate that the new design also achieves greater excitation homogeneity along the z-direction, providing stronger and more uniform field amplitudes at increased imaging depths.

3.2 Imaging Simulations

To better understand and optimize imaging with our single-sided MPI scanner, a series of numerical simulations were developed to replicate the imaging process. These simulations were used during early system development, as the unique hardware configuration of our scanner required imaging methodologies distinct from those used in conventional closed-bore MPI systems. By simulating the imaging process, we were able

to rapidly prototype new imaging schemes, evaluate their feasibility, and identify acquisition strategies that were most compatible with our scanner geometry and field topology.

In addition to early prototyping, the imaging simulations also serve as a numerical tool to understand the physical principles of image formation in our system. They provide a framework to visualize how the FFL is scanned, and how image sensitivity and spatial resolution vary with position. This section describes the design and implementation of these simulations, explains how they replicate the physical operation of the scanner, and presents representative results that illustrate the imaging process and system behavior.

3.2.1 Magnetic Field Loading

Simulating the magnetic fields produced by each coil using the Biot–Savart law is computationally expensive and therefore impractical to perform repeatedly during imaging simulations. Instead, the magnetic fields generated by each coil are simulated once, as described in the previous subsections, and saved. These precomputed field maps are then loaded at the start of the imaging simulation scripts. The fields are simulated over a predefined FOV that encompasses the expected imaging region and are reused by all higher-level simulations.

For the purpose of simulating the signal generated by an SPIO sample, only the magnetic field at the locations occupied by SPIO particles is required. Magnetic fields at positions without SPIO do not contribute to the detected signal. Accordingly, the user specifies a set of voxel locations corresponding to the SPIO distribution, and the magnetic field at each voxel location is obtained by interpolating the loaded field maps.

All magnetic field maps are simulated assuming a DC current of $I = 1$ A in each coil. The magnetic field produced by a given coil at an arbitrary current is obtained by scaling the corresponding unit-current field map. The total selection field is therefore given by

$$\mathbf{B}_{\text{sel}}(\mathbf{r}) = I_1 \mathbf{P}_1(\mathbf{r}) + I_2 \mathbf{P}_2(\mathbf{r}) + I_3 \mathbf{P}_3(\mathbf{r}), \quad (3.3)$$

where $\mathbf{P}_i(\mathbf{r})$ represents the magnetic field per unit current produced by coil i , imported from its corresponding Biot–Savart simulation file. The relative magnitudes of the currents I_1 , I_2 , and I_3 determine the position FFL.

The excitation field is time-varying and is applied to drive the nonlinear magnetization response of the SPIO sample. It is expressed as

$$\mathbf{B}_{\text{ex}}(\mathbf{r}, t) = I_{\text{peak}} \cos(\omega_1 t) \mathbf{P}_{\text{ex}}(\mathbf{r}), \quad (3.4)$$

where $\mathbf{P}_{\text{ex}}(\mathbf{r})$ is the excitation coil field per unit current, also loaded from a precomputed simulation file.

The total magnetic field applied to an SPIO voxel is the superposition of the selection and excitation fields,

$$\mathbf{B}(\mathbf{r}, t) = \mathbf{B}_{\text{sel}}(\mathbf{r}) + \mathbf{B}_{\text{ex}}(\mathbf{r}, t), \quad (3.5)$$

where the time dependence arises solely from the excitation field, while the selection field provides a spatially varying DC offset. This total magnetic field serves as the input to the subsequent stages of the simulation, which calculate the magnetization response of the SPIO sample and the resulting induced voltage in the receive coil.

3.2.2 Signal Detection Simulation

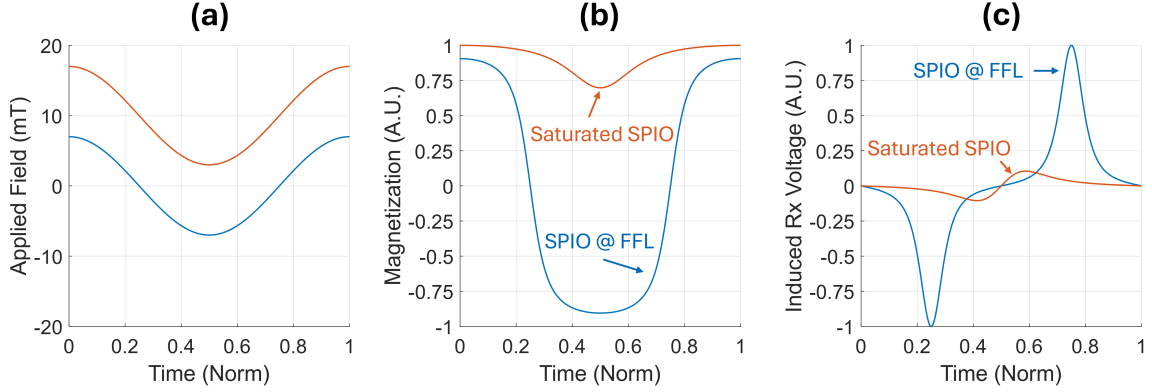


Figure 3.5: **Simulated signal detection chain.** (a) Applied magnetic field as a function of time for two SPIO locations: particles located at the field-free line (FFL), experiencing only the excitation field (blue), and particles located away from the FFL, experiencing both the excitation field and a nonzero selection field offset (orange). (b) Resulting SPIO magnetization response calculated using the Langevin model for the two applied field conditions. SPIO at the FFL exhibits a strongly nonlinear magnetization response, while SPIO outside the FFL remains largely saturated. (c) Induced voltage in the receive coil caused by the oscillating magnetization. A strong signal is generated only by SPIO located near the FFL.

To model signal detection, which serves as the basis for the higher-level imaging simulations presented later in this section, SPIO excitation and receive coil detection are simulated³. Given the total magnetic field $\mathbf{B}(\mathbf{r}, t)$ calculated as described in Sec. 3.2.1, the SPIO magnetization response and induced receive signal are computed. The magnetization $\mathbf{M}(\mathbf{r}, t)$ is described using the Langevin model of superparamagnetism,

³The MATLAB implementation of the signal detection simulation is provided in Appendix B.2.

$$\mathbf{M}(\mathbf{B}(\mathbf{r}, t)) = c(\mathbf{r}) \frac{m}{\mu_0} \mathcal{L} \left(\frac{\beta |\mathbf{B}(\mathbf{r}, t)|}{\mu_0} \right) \hat{\mathbf{B}}(\mathbf{r}, t), \quad (3.6)$$

where $c(\mathbf{r})$ is the particle concentration, m is the magnetic moment of a single particle, and $\mathcal{L}$ denotes the Langevin function. Because the magnetization depends nonlinearly on a numerically defined magnetic field, the time derivative $\partial \mathbf{M} / \partial t$ is evaluated numerically. In the simulations, this derivative is computed using a finite-difference approximation,

$$\frac{\partial \mathbf{M}(\mathbf{r}, t_k)}{\partial t} \approx \frac{\mathbf{M}(\mathbf{r}, t_{k+1}) - \mathbf{M}(\mathbf{r}, t_k)}{\Delta t}, \quad (3.7)$$

where t_k denotes the discrete time samples and Δt is the temporal sampling interval.

The induced voltage in the receive coil is proportional to the time derivative of the magnetization, weighted by the spatial sensitivity profile of the receive coil. Using the reciprocity principle, this relationship can be expressed as

$$u(\mathbf{r}_{\text{FFL}}, t) \propto \mathbf{P}_{\text{rx}}(\mathbf{r}) \cdot \frac{\partial \mathbf{M}(\mathbf{r}, t)}{\partial t}, \quad (3.8)$$

where $\mathbf{P}_{\text{rx}}(\mathbf{r})$ is the magnetic field produced by the receive coil per unit current, obtained from the Biot–Savart simulations described in Sec. 3.1.3.

More generally, the total induced voltage can be written as a spatial integral over the SPIO distribution Eq. 2.9,

$$u(\mathbf{r}_{\text{FFL}}, t) = - \int \mathbf{P}_{\text{rx}}(\mathbf{r}) \cdot \frac{\partial \mathbf{M}(\mathbf{r}, t)}{\partial t} dV, \quad (3.9)$$

which represents the superposition of signals from all SPIO particles within the imaging volume. In the simulations, this integral is implemented as a discrete summation over all SPIO voxels,

$$u(\mathbf{r}_{\text{FFL}}, t) = -dV \sum_i \mathbf{P}_{\text{rx}}(\mathbf{r}_i) \cdot \frac{\partial \mathbf{M}(\mathbf{r}_i, t)}{\partial t}. \quad (3.10)$$

Figure 3.5 illustrates the simulated signal generation process for two SPIO voxel locations, one positioned in the FFL and one located away from it. When located in the FFL, the SPIO voxel experiences no selection field offset and is driven solely by the excitation field, resulting in a strongly nonlinear oscillation of the magnetization and a large induced voltage in the receive coil. In contrast, an SPIO voxel located away from the FFL experiences a substantial DC offset from the selection field, causing its magnetization to remain largely saturated and yielding a significantly weaker receive signal. This contrast in signal amplitude as a function of SPIO position demonstrates the spatial encoding used for image formation in MPI.

3.2.2.1 Single Harmonic Measurement The induced voltage shown in Eq. 3.10 is a time-varying signal composed of multiple harmonics of the excitation frequency. For imaging, this voltage is not used directly; instead the signal is reduced to a single harmonic component, as discussed in Sec. 2.4.

In experimental measurements, this harmonic isolation is performed using a lock-in amplifier. In the simulations, the same operation is implemented numerically by computing the discrete Fourier coefficients of the simulated receive voltage $u(t)$ over one excitation period. For a discretely sampled waveform $u(t_i)$ with $i = 1, \dots, N$, the Fourier coefficients are given by

$$a_n = \frac{2}{N} \sum_{i=1}^N u(t_i) \cos(n\omega_1 t_i), \quad (3.11)$$

$$b_n = \frac{2}{N} \sum_{k=1}^N u(t_k) \sin(n\omega_1 t_i), \quad (3.12)$$

where n denotes the harmonic index. Throughout this work, the third harmonic ($n = 3$) is used as the signal metric. Due to the symmetry of the SPIO response, the cosine coefficient a_3 is zero, and the simulated signal is fully characterized by the sine coefficient b_3 . The resulting harmonic values are used directly in the subsequent imaging simulations.

3.2.3 One-Dimensional Projection Imaging Simulation

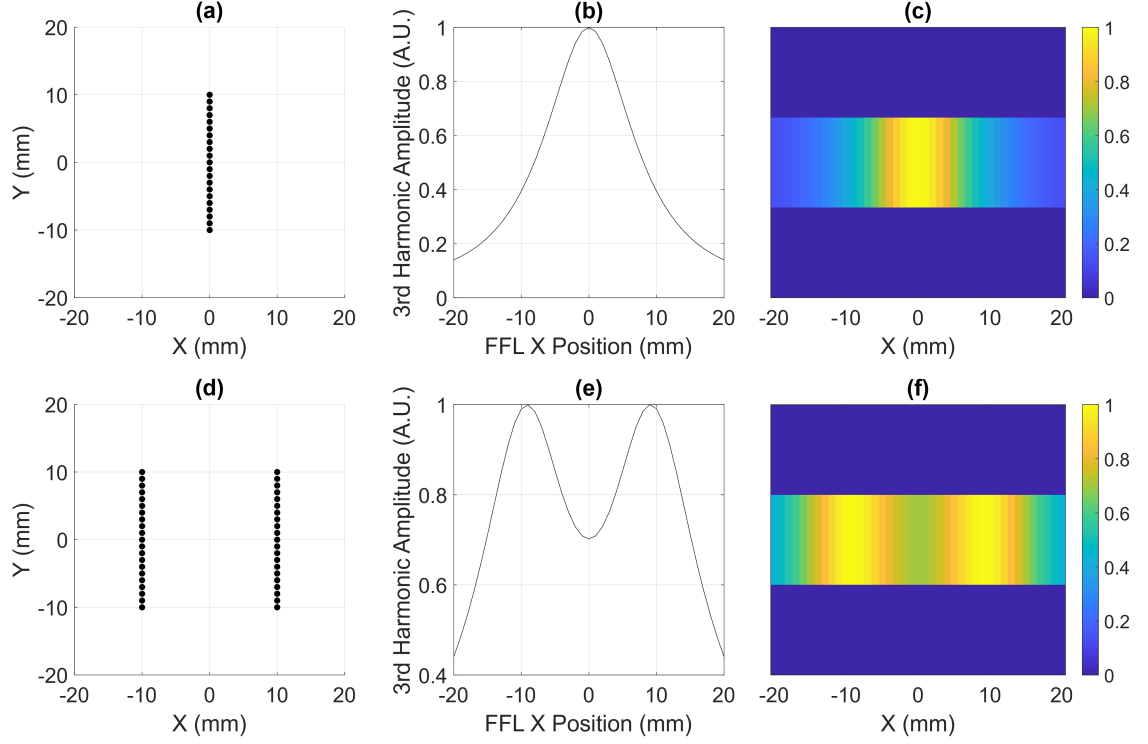


Figure 3.6: **One-dimensional projection imaging simulation.** (a) Simulated SPIO voxel locations in the XY-plane forming a single line phantom centered at $x = 0$. (b) Simulated one-dimensional projection signal obtained by scanning the FFL across the single-line phantom in the x -direction. (c) One-dimensional projection image formed from the simulated projection data in (b). (d) Simulated SPIO voxel locations in the XY-plane forming a dual line phantom with rods located at $x = -10$ mm and $x = 10$ mm. (e) Simulated one-dimensional projection signal obtained by scanning the FFL across the dual line phantom. (f) One-dimensional projection image corresponding to the projection data in (e).

The simplest form of the imaging simulations implemented in this work is 1D projection imaging⁴. This simulation represents the base level of image formation used throughout the remainder of this chapter, with higher-dimensional imaging building upon this framework. In 1D projection imaging, the FFL is scanned laterally across the FOV along the x -axis, and the detected signal is recorded as a function of FFL position. At each FFL location, the signal metric is taken as the amplitude of the third harmonic of the receive voltage, as described in Sec. 3.2.2.

Numerically, this is achieved by evaluating the signal detection simulation at multiple discrete FFL positions. The FFL position is changed by changing the selection coil currents, which causes the FFL to translate laterally across the imaging region while the excitation field remains unchanged. The selection field $\mathbf{B}_{\text{sel}}(\mathbf{r})$ is determined by the applied selection coil currents according to Eq. 3.3, which defines the instantaneous FFL position. Multiple algorithms have been developed to precisely control the position of the FFL, which will be described later in this work.

For a given FFL position, the magnetic fields at each SPIO voxel are computed and passed to the signal detection simulation described previously. The resulting time-domain receive signal is processed to extract the third harmonic amplitude, yielding a single scalar value representing the detected signal at that FFL location. Repeating this process for all FFL positions produces a 1D projection of the SPIO distribution.

Figure 3.6 illustrates this process for two simple simulated phantoms. Panels (a)–(c) show the results for a single-line phantom centered at $x = 0$, while panels (d)–(f) show the corresponding results for a dual-line phantom with rods located at $x = \pm 10$ mm. The resulting 1D projection signals exhibit peaks corresponding to the lateral positions of the SPIO lines. These simulations provide a foundational validation of the signal model

⁴The MATLAB implementation of the one-dimensional projection imaging simulation is provided in Appendix B.3.

and scanning methodology and serve as the basis for the higher-dimensional imaging simulations presented in the following sections.

3.2.4 Two Dimensional (XY) Tomographic Simulations

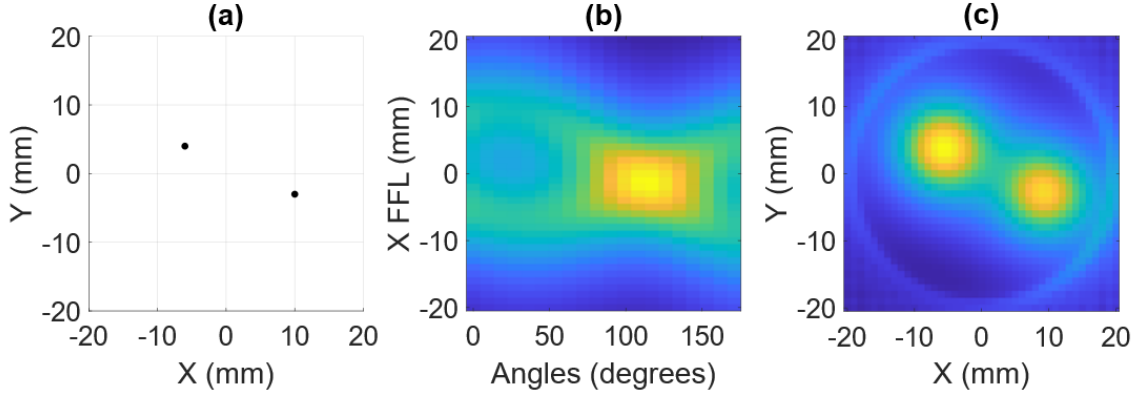


Figure 3.7: **Two-dimensional XY imaging simulation.** (a) Simulated SPIO phantom in the XY-plane consisting of two point-like sources at a fixed height ($z = 17$ mm). (b) Simulated sinogram formed by rotating the phantom over 20 projection angles spanning 0 – 180° and, for each angle, acquiring a 1D projection by scanning the FFL along x from -20 to 20 mm in 1 mm steps. (c) Reconstructed XY image obtained from the sinogram using filtered backprojection (iradon MATLAB function, with Hann filter).

Two-dimensional imaging in the XY-plane is achieved by rotating the phantom relative to the scanner geometry⁵. Rotating the phantom allows the same object to be imaged at multiple projection angles without altering the FFL trajectory or scanning strategy. In the simulations, this rotation is implemented by applying a planar rotation

⁵The MATLAB implementation of the two-dimensional XY tomographic imaging simulation is provided in Appendix B.4.

matrix to the SPIO voxel coordinates in the XY-plane for each projection angle,

$$\begin{pmatrix} x' \\ y' \end{pmatrix} = \begin{pmatrix} \cos \theta & -\sin \theta \\ \sin \theta & \cos \theta \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix}, \quad (3.13)$$

while keeping the z -coordinate fixed. For each rotated phantom configuration, a full 1D projection is acquired by scanning the FFL laterally across the FOV, as described in Sec. 3.2.3.

Repeating the 1D projection imaging process over multiple projection angles produces a sinogram, with each column corresponding to a single projection angle and each row corresponding to an FFL position along x . This sinogram encodes the spatial distribution of SPIO within the XY-plane. Reconstruction of the two-dimensional image is performed using filtered backprojection, as described in Sec. 2.5.1. Figure 3.7 shows an example of this process for a simple two-point phantom.

3.2.5 Two Dimensional (XZ) Projection Simulations

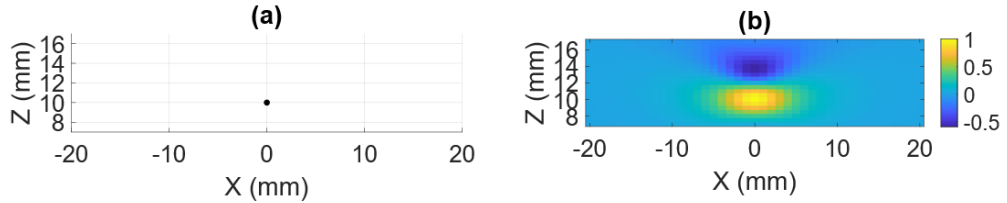


Figure 3.8: **Two-dimensional XZ imaging simulation.** (a) Simulated SPIO phantom in the XZ-plane consisting of a single point source. (b) Simulated XZ projection image obtained by acquiring 1D projections at multiple phantom heights.

Two dimensional imaging in the XZ-plane follows the same approach as the XY tomographic simulations described above with one difference⁶. Instead of rotating the phantom to acquire angular projections the phantom is translated mechanically along the z -direction. All other aspects of the simulation including FFL scanning along x , signal detection, and harmonic extraction are identical to those used for XY imaging.

For each phantom height a full 1D projection is acquired by scanning the FFL laterally across the FOV as described in Sec. 3.2.3. The FFL remains fixed at a height of $z = 17$ mm and translating the phantom allows the same FFL trajectory to probe different depths within the imaging volume. Repeating this process for a sequence of phantom heights produces a set of 1D projections indexed by z which are stacked to form a 2D XZ projection image. No further reconstruction is done to form these images.

Unlike the XY imaging simulations these images are not tomographic reconstructions. Instead they represent projection images analogous to conventional x-ray imaging where each pixel corresponds to a line integral along the projection direction. Figure 3.8 shows an example of this process for a single point source of SPIO. The resulting XZ projection image exhibits a strong positive signal at the SPIO location accompanied by negative lobes at heights above and below the particle. These features arise from the axial structure of the third-harmonic PSF along the z -direction. The presence of these negative lobes can lead to signal contamination from out of plane SPIO demonstrating a fundamental limitation of single harmonic imaging using the third harmonic.

3.3 Machine Learning Enhancements

This section explores the use of machine learning as a complementary approach for improving image reconstruction for single-sided MPI systems. Due to the inherent

⁶The MATLAB implementation of the two-dimensional xz projection imaging simulation used throughout this work is provided in Appendix B.5.

magnetic field inhomogeneity, leading to shift variance, conventional analytical reconstruction techniques can produce artifacts and spatial distortions that are difficult to fully mitigate through hardware design or imaging procedure alone. Machine learning offers an alternative means of addressing these challenges by learning system-specific corrections from simulated data.

Using simulated datasets generated from the imaging models described earlier in this chapter, neural networks are investigated for their ability to correct for inhomogeneities in the system, and their performance is assessed on both sinograms and reconstructed images. In addition to demonstrating improvements to simulated data, this section also examines the limitations of applying simulation trained networks to experimental data and discusses possible directions for future development.

3.3.1 Motivation

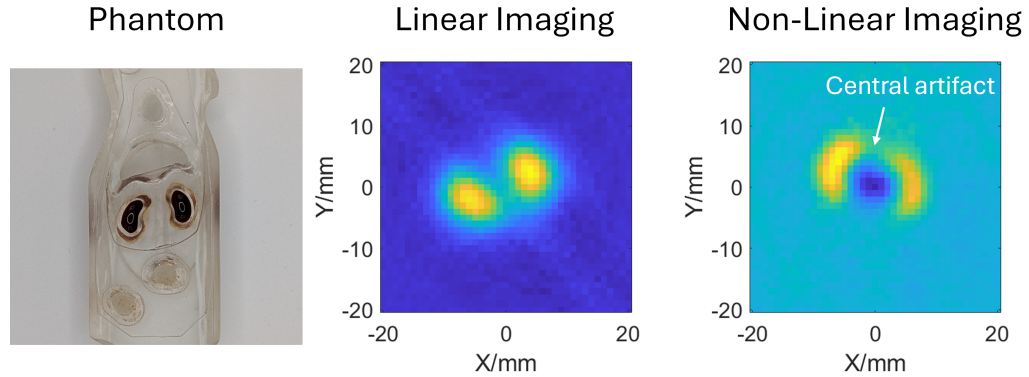


Figure 3.9: **Reconstruction artifacts due to field inhomogeneity.** Left: photograph of the mouse kidney phantom used for imaging. Center: MPI reconstruction acquired using a homogeneous selection-field gradient across the FOV. Enforcing gradient homogeneity suppresses artifacts originating from inhomogeneities but requires reducing the gradient strength, resulting in reduced spatial resolution. Right: MPI reconstruction of the same phantom acquired using a non-homogeneous scanning strategy in which the maximum achievable gradient is used at each FFL position. While this approach improves local sharpness, it introduces a negative spot artifact near the center of the FOV, highlighted in the image.

Image reconstruction in single-sided MPI is fundamentally challenging due to the inherent magnetic field inhomogeneity arising from the scanner geometry. As a consequence, the system response is inherently shift-variant, with both signal strength and spatial resolution depending on position within the FOV. This violates the assumptions underlying many standard reconstruction techniques which assume a linear shift-invariant (LSI) system, including FBP. When applied to a shift-variant system, can produce non-trivial artifacts and spatial distortions that compromise image fidelity. Deconvolution techniques such as Lucy–Richardson or Wiener deconvolution are particularly sensitive to

this issue, as they rely on a spatially invariant PSF and therefore tend to perform poorly under field inhomogeneity.

Figure 3.9 demonstrates this behavior for reconstructions acquired using a non-homogeneous scanning strategy in which the selection field gradient is not normalized across the FOV. In this case, the maximum achievable gradient is used at each FFL position rather than enforcing a constant gradient over the scan range. While this approach enables larger FOV while still maintaining higher local gradient strengths, it is highly inhomogeneous imaging technique, resulting in a non-trivial central negative artifact.

One way to reduce shift variance of single-sided systems is to impose "semi-homogeneity" through hardware and software constraints. On the hardware side, coil designs can be optimized to produce semi-homogeneous magnetic fields over a limited region, as demonstrated by the surface excitation coil discussed in Sec. 3.1.4. However, such approaches will never make the fields perfectly homogeneous without compromising the single-sided geometry. On the software side, pulse sequences can be constructed to maintain a constant selection field gradient across all FFL positions. Although this improves encoding uniformity, it introduces a tradeoff between FOV and gradient strength. Enforcing gradient homogeneity over a larger scan range requires reducing the maximum gradient, which directly limits spatial resolution, particularly near the center of the FOV. Thus, removing the LSI constraint would allow for imaging over large FOVs without compromising high spatial resolution in the center of the scanner.

Machine learning provides an alternative reconstruction approach that does not rely on enforcing homogeneity, since no assumption of LSI is made. By training on representative simulated data, the neural network can learn the spatially varying relationship between measured signals and phantom geometry, allowing reconstruction to adjust for system inhomogeneities. Promising elimination of artifacts in the reconstructed images originating from those inhomogeneities. In addition to artifact suppression, this

approach shows potential to improve spatial fidelity through implicit, position-dependent deconvolution and to reduce noise through nonlinear denoising, motivating its exploration for single-sided MPI.

3.3.2 Network Use for Sinogram Cleaning

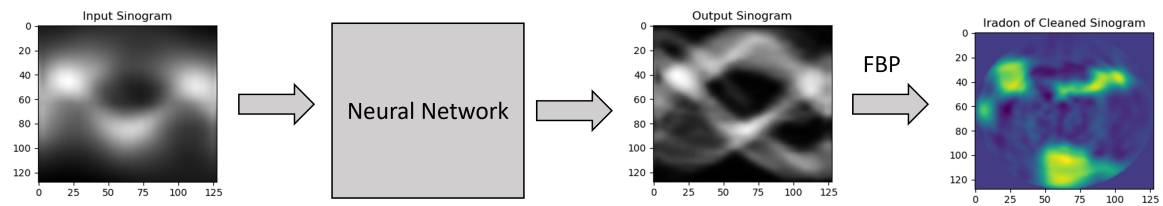


Figure 3.10: **Sinogram cleaning using a neural network.** Schematic of the sinogram cleaning approach used in this work. A neural network is trained to map measured pseudo-sinograms, distorted by magnetic field inhomogeneity causing a position-dependent PSF, to cleaned sinograms that more closely approximate the sinograms produced by an ideal Radon imager. The cleaned sinograms are then reconstructed using FBP.

Rather than attempting to replace the entire image reconstruction pipeline, machine learning is applied here as an intermediate processing step that operates directly on the sinogram. The goal of this approach is to transform the measured "pseudo-sinograms" produced by our scanner into "true-sinograms" which are simply ideal Radon transforms of the imaged object. Essentially, removing inhomogeneity and performing deconvolution before FBP reconstruction. The overall processing strategy is illustrated in Fig. 3.10.

In an ideal line-based imaging system, the measured sinogram corresponds directly to the Radon transform of the object, enabling accurate reconstruction using FBP. In practice, all imaging systems deviate from this ideal behavior. Even in LSI systems, the

measured signal is a convolution of the ideal projection with the system PSF. In our scanner, magnetic field inhomogeneity introduces additional spatial dependence, resulting in a spatially varying PSF. As a result, the measured pseudo-sinograms differ substantially from the ideal Radon transform. These deviations propagate through reconstruction and manifest as artifacts, spatial distortion, and signal broadening, degrading spatial fidelity.

The neural network is trained to learn a mapping between distorted pseudo-sinograms and ideal sinograms generated from simulated phantoms using the Radon transform. After this sinogram cleaning step, the corrected sinograms are reconstructed using standard FBP. Restricting the network's role to sinogram correction keeps the reconstruction based in well-established analytical methods while reducing the complexity of the learning task. Operating in sinogram space hopefully allows the network to directly compensate for position-dependent distortions arising from the shift-variant encoding of the scanner.

3.3.3 Dataset Generation Simulation

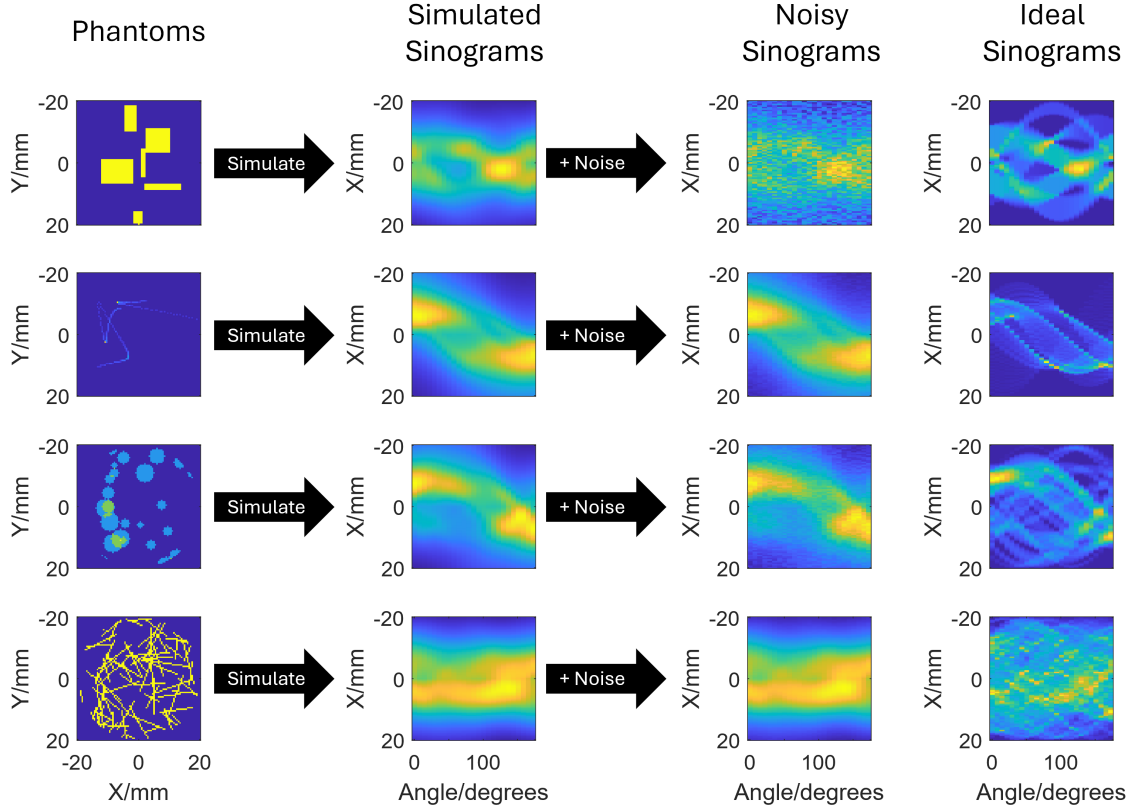


Figure 3.11: **Simulated dataset generation for network training.** Representative training samples illustrating the dataset generation pipeline. Left column: randomly generated two-dimensional phantoms in the XY plane. Second column: corresponding pseudo-sinograms produced by the imaging simulations described in Sec. 3.2. Third column: noisy pseudo-sinograms obtained by adding Gaussian noise to approximate experimental measurement. Right column: ideal sinograms of the same phantoms, computed using the Radon transform.

A large training dataset is necessary for supervised neural network methods.

Ideally, such a dataset would consist of experimental measurements, since real data

naturally include system specific effects and anomalies. However, this is not feasible here. MPI remains an early stage imaging modality with limited standardization, moreover our single-sided scanner is unique among scanners. Consequently, no large experimental dataset exists for training. To address this limitation, all machine learning models in this work are trained using synthetically generated data generated using the imaging simulations described in Sec. 3.2.

Training data are generated by first constructing two-dimensional phantoms representing arbitrary SPIO distributions in the XY plane. These phantoms are created using a combination of simple geometric shapes (e.g., points, lines, rods, and clustered structures) and randomized spatial patterns to ensure diversity in shape, scale, and edge characteristics. This diversity reduces the risk of overfitting to a narrow class of object geometries.

For each phantom, image acquisition is simulated using the XY imaging simulations described in Sec. 3.2.4. Specifically, a pseudo-sinogram is generated using 25 projection angles spanning 0° to 180° and 81 discrete FFL positions spanning -20 to 20 mm, with uniform spacing in both angle and position. After generation of each pseudo-sinogram, additive Gaussian noise is applied with a magnitude randomly selected between -10 and -50 dB to approximate electronic noise in the experimental system. The resulting noisy pseudo-sinograms are intended to mimic the measurements acquired on the physical scanner and therefore serve as inputs to the neural network.

To generate the corresponding ideal sinograms (the desired network outputs), a Radon transform is taken of each phantom. This provides the sinogram that would be obtained by an ideal line-based imaging system, in which the PSF is a delta function and the imaging is LSI. Pairing each noisy pseudo-sinogram with its corresponding Radon sinogram yields the input target training pairs used for network training. Figure 3.11

shows representative examples, demonstrating the diversity of phantom geometries and the corresponding pseudo and ideal sinograms.

3.3.4 Neural Network Architectures Considered

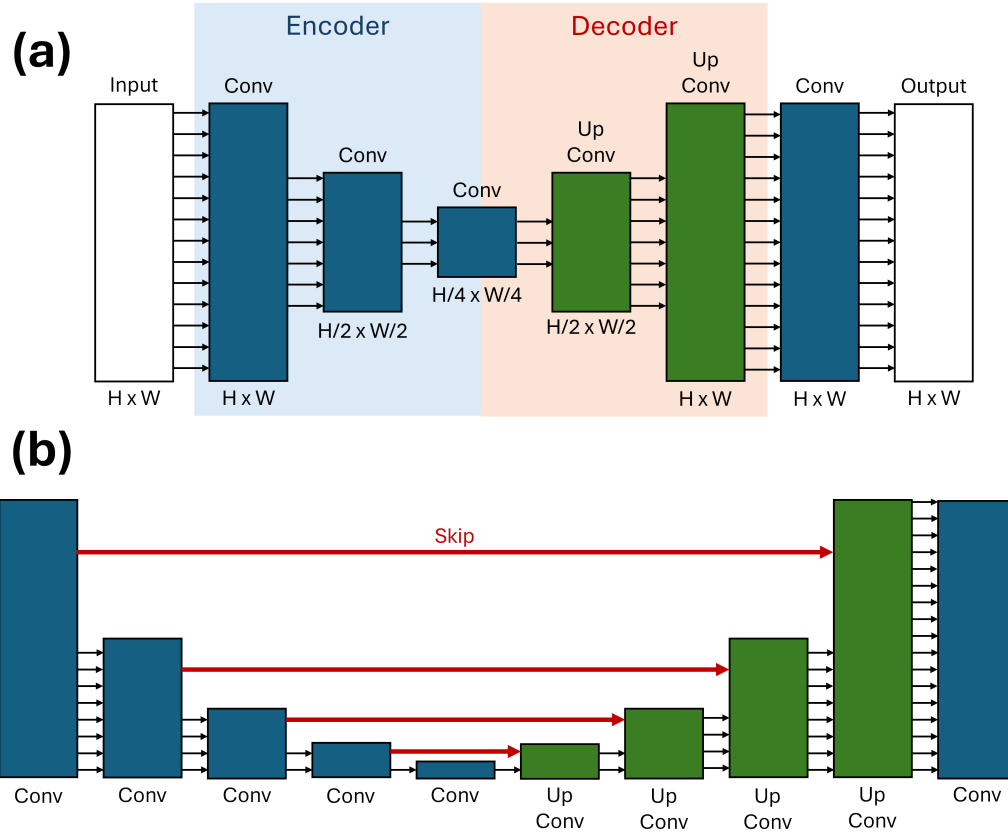


Figure 3.12: **Neural network architectures considered.** Conceptual comparison of the two neural network architectures evaluated in this work. (a) A basic convolutional autoencoder consisting of an encoder, a low-dimensional latent representation, and a decoder. (b) A U-Net architecture with a symmetric encoder–decoder structure and skip connections that propagate fine-scale spatial features from the encoder directly to the decoder.

Two convolutional neural network architectures were investigated for sinogram cleaning, a basic convolutional autoencoder [80] and a U-Net [81]. Both networks operate directly on two-dimensional sinograms and are trained to map distorted pseudo-sinograms to ideal sinograms generated from simulated phantoms. Although both architectures follow an encoder–decoder paradigm, they differ in how spatial information is preserved during reconstruction.

Autoencoders encourage the network to learn global, higher-order structure by forcing the input data through a reduced latent space. This bottleneck reduces dimensionality and promotes suppression of noise and redundant information, which makes autoencoders effective for tasks such as classification and feature extraction. However, this same compression can discard fine spatial detail. For imaging tasks that require preservation of localized structures, the bottleneck often leads to overly smooth or block-like reconstructions, limiting performance when sharp features must be retained.

In contrast, the U-Net augments the encoder–decoder structure with skip connections that directly link corresponding encoding and decoding layers. These connections allow high-resolution spatial information to bypass the bottleneck, enabling the network to preserve localized features while still learning global context. This architectural difference makes the U-Net better suited for tasks such as image reconstruction, as a result this architecture is used for many biomedical applications.

In the implementations used here, the autoencoder consists of a shallow encoder–decoder structure with two convolutional blocks. Each block uses 3×3 convolutional kernels with 32 feature channels and ReLU activation, followed by 2×2 max-pooling in the encoder and transposed convolutions in the decoder. A final 3×3 convolution with sigmoid activation produces the cleaned sinogram.

The U-Net architecture is also symmetric, but consists of more layers. The encoder begins with 16 feature channels and doubles at each downsampling step, reaching

256 channels at the bottleneck. Each encoding level consists of two 3×3 convolutional layers with ReLU activation followed by max-pooling. The decoder mirrors this structure using up-convolutions and concatenation with the corresponding encoder feature maps. Dropout is applied at deeper layers to reduce overfitting, and a final 1×1 convolution with sigmoid activation produces the output sinogram.

These architectural differences influence reconstruction performance. The autoencoder's reduced dimensionality limits its ability to preserve fine spatial structure, while the U-Net's skip connections allow recovery of localized sharp features. These differences are examined in the following sections through direct comparison of cleaned sinograms and reconstructed images.

3.3.5 Training Strategy and Loss Functions

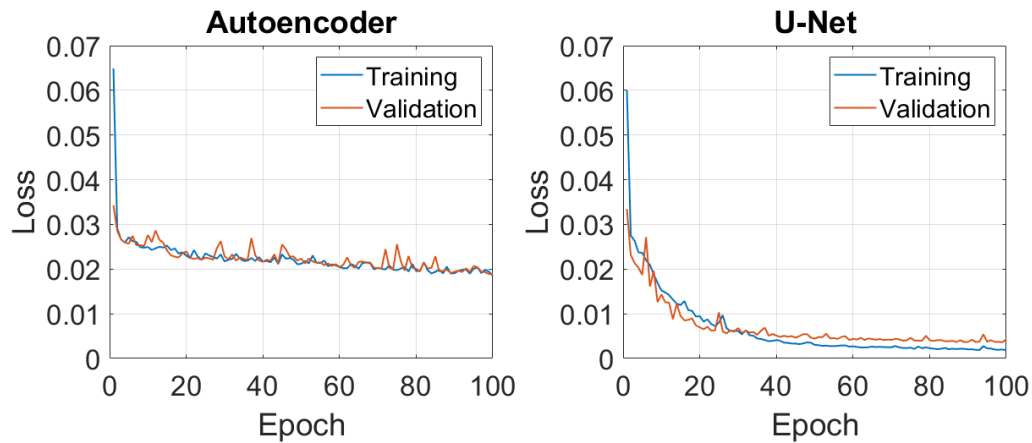


Figure 3.13: **Training loss during network optimization.** Training and validation loss as a function of epoch for the autoencoder and U-Net networks. Loss values are computed using mean squared error (MSE).

Both networks were trained using the same supervised learning protocol, with paired sinograms serving as inputs and targets. Each training sample consisted of a noisy pseudo-sinogram as the network input and the corresponding ideal sinogram as the training target. During training, both input and target sinograms were normalized by their maximum absolute value to constrain pixel values to the range $[-1, 1]$. This normalization improves numerical stability during optimization and ensures that the loss function is not dominated by variations in absolute signal amplitude across training samples.

All models were implemented in Keras and trained using the Adam optimizer with a mean squared error (MSE) loss function. The MSE loss was selected because the sinogram-cleaning task is a regression problem in which the network output is expected to approximate the ideal sinogram on a pixel-by-pixel basis. For a predicted sinogram $\hat{S}$ and corresponding ideal sinogram S , each containing N pixels, the MSE loss is defined as

$$\text{MSE} = \frac{1}{N} \sum_{i=1}^N (\hat{S}_i - S_i)^2. \quad (3.14)$$

This loss function penalizes large deviations between the predicted and ideal sinograms while treating all pixels uniformly. Pushing the network to output the ideal sinogram.

Training data were loaded from a directory containing 1000 MATLAB .mat files, each containing a training pair. The dataset was randomly shuffled and partitioned into three non-overlapping subsets: 70% for training, 15% for validation, and 15% for testing. Networks were trained for 100 epochs using a mini batch size of 8. Validation loss was evaluated once per epoch using the validation subset, providing a quantitative measure of performance throughout training. For each epoch, the number of parameter update steps was determined by the size of the training set and the selected batch size.

Figure 3.13 shows the training and validation loss curves for both architectures. In both cases, the loss decreases rapidly during early epochs and then gradually approaches a plateau, indicating stable convergence. The absence of a strong divergence between

training and validation loss suggests that overfitting is limited. Differences in convergence rate and final validation loss reflect differences in model complexity and are examined in the following sections through direct comparison of cleaned sinograms and reconstructed images.

3.3.6 Network Comparison Sinograms

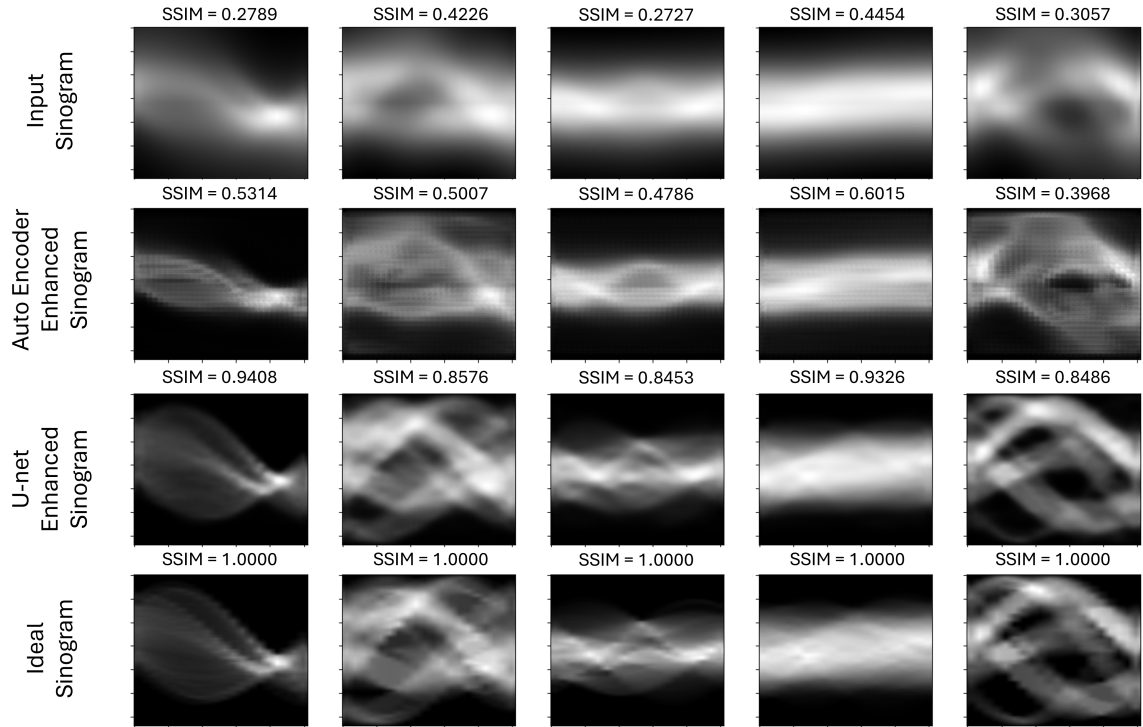


Figure 3.14: **Comparison of sinogram enhancement by neural networks.** Sinograms illustrating the performance of the two network architectures. Top row: input noisy pseudo-sinograms generated using the imaging simulations. Second row: sinograms enhanced using the autoencoder. Third row: sinograms enhanced using the U-Net. Bottom row: ideal sinograms obtained from the Radon transform of the corresponding phantoms. Structural similarity index (SSIM) values with respect to the ideal sinograms are shown above each image.

Figure 3.14 compares the sinogram enhancement performance of the autoencoder and the U-Net using representative samples. To quantify similarity between enhanced sinograms and their corresponding ideal sinograms, the structural similarity index (SSIM) is used. SSIM is an image similarity metric that quantifies differences in local signal statistics and spatial structure between two images, making it useful for comparing ideal sinograms with their network enhanced counterparts. For two images X and Y , SSIM is defined as

$$\text{SSIM}(X, Y) = \frac{(2\mu_X\mu_Y + C_1)(2\sigma_{XY} + C_2)}{(\mu_X^2 + \mu_Y^2 + C_1)(\sigma_X^2 + \sigma_Y^2 + C_2)}, \quad (3.15)$$

where μ_X and μ_Y are the mean intensities of the images, σ_X^2 and σ_Y^2 are the variances, and σ_{XY} is the covariance between X and Y . The constants C_1 and C_2 stabilize the metric for small denominators. SSIM values range from -1 to 1 , with 1 indicating perfect structural agreement.

Quantitatively, both network architectures improve the similarity of the input pseudo-sinograms to the ideal sinograms, as evidenced by increased SSIM values for all enhanced examples shown in Fig. 3.14. In all cases, the U-Net achieves higher SSIM values than the autoencoder, indicating superior structural agreement with the ideal sinograms. However, neither architecture achieves perfect agreement ($\text{SSIM} = 1$), caused by the complexity of the task and the approximate nature of machine learning approaches.

Qualitative inspection of the sinograms supports these observations as well. Both networks reduce noise and recover correct sinogram features, making them appear more like the ideal sinogram. The autoencoder enhanced sinograms exhibit reduced spatial fidelity, with visible discretization artifacts and spurious features. This behavior is expected due to the dimensionality reducing bottleneck inherent to autoencoder architectures, which can lead to loss of fine spatial information. In contrast, the U-Net produces smoother and more structurally correct sinograms that more closely resemble the

target ideal sinogram. This improvement is attributed to the presence of skip connections, which allow smaller spatial features to propagate directly through the network.

Overall, Fig. 3.14 demonstrates that neural networks are appropriate for this task and are capable of performing effective sinogram correction, including partial deconvolution and compensation for field inhomogeneity in simulated data. Specifically, the U-Net architecture shows the most promise for this task, consistent with its successful application in other biomedical imaging modalities. How these sinogram improvements carry over to the reconstructed image quality is explored in the following subsection.

3.3.7 Network Comparison Reconstructed Images

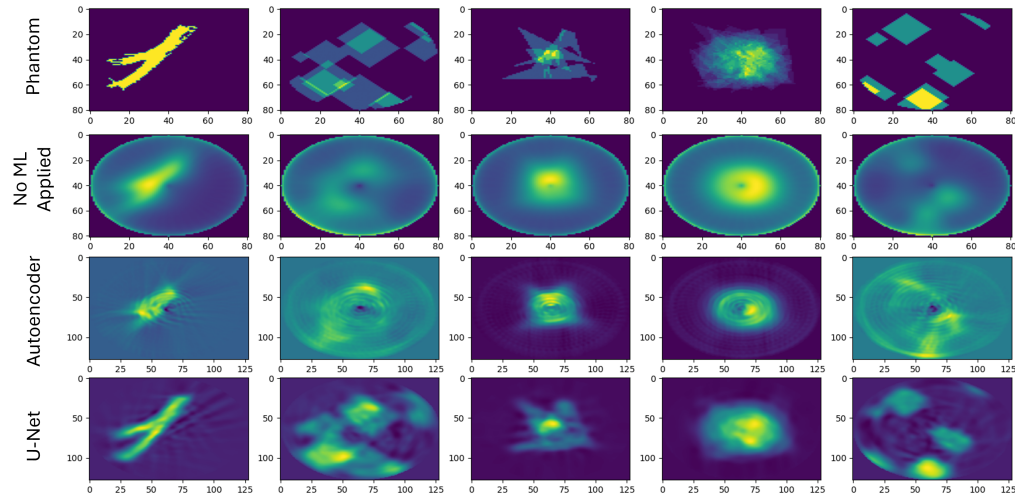


Figure 3.15: **Comparison of reconstructed images with machine learning enhancements.** FBP reconstructions corresponding to the sinograms shown in Fig. 3.14. Top row: ground truth phantoms. Second row: reconstructions obtained from unprocessed noisy pseudo-sinograms. Third row: reconstructions obtained from autoencoder enhanced sinograms. Bottom row: reconstructions obtained from U-Net enhanced sinograms.

Figure 3.15 compares reconstructed images obtained using FBP applied to sinograms before and after machine learning enhancement. In contrast to the previous subsection, which quantitatively evaluated network performance in the sinogram domain, this section provides a qualitative assessment of the reconstructed images.

Reconstructions obtained without sinogram cleaning exhibit degraded spatial resolution, spatially varying intensity, and artifacts that compromise image fidelity. In particular, SPIO near the center of the FOV appear artificially brighter than those near the periphery, with additional halo artifacts at the edges of the FOV and a negative central artifact, as shown in Fig. 3.15. Applying sinogram cleaning prior to reconstruction substantially reduces these artifacts and improves spatial resolution, allowing the phantom geometries to be more clearly resolved.

Consistent with the sinogram comparison results, the U-Net provides superior reconstruction performance compared to the autoencoder. Reconstructions enhanced by the U-Net exhibit improved spatial resolution, increased image uniformity, and more effective artifact suppression. Notably, the negative central artifact is fully suppressed in all U-Net-enhanced reconstructions shown, whereas residual distortions remain in the autoencoder enhanced reconstructions. This behavior is expected, as the skip connections in the U-Net architecture better preserve spatial information leading to better performance.

Overall, these reconstructed images demonstrate the potential of neural networks to address challenges associated with imaging in a non-LSI system. The results show that machine learning sinogram correction can compensate for field inhomogeneity and substantially reduce reconstruction artifacts, particularly when using a U-Net architecture. The following subsection examines the application of this approach to experimental data and discusses its limitations and future directions.

3.3.8 Application to Real Data and Future Directions

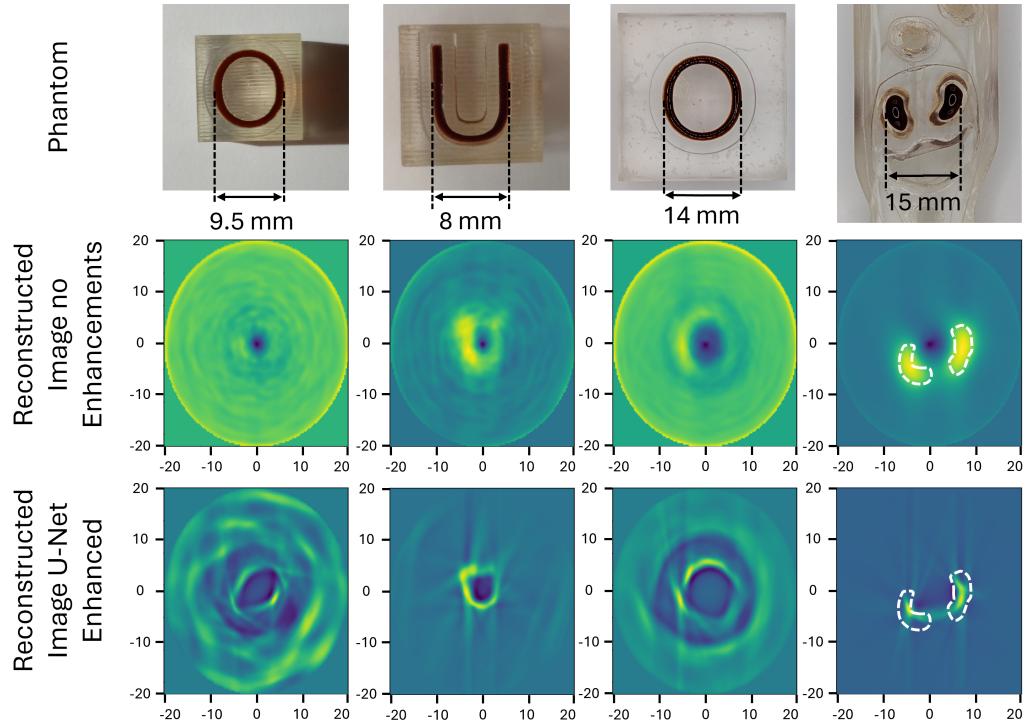


Figure 3.16: **Application of the U-Net to experimental data.** Reconstructed images of experimental phantoms. Top row: photographs of the physical phantoms. Second row: FBP reconstructions obtained from unprocessed experimental sinograms. Third row: FBP reconstructions obtained after U-Net–based sinogram enhancement.

While the U-Net network demonstrated strong performance when applied to simulated datasets, its performance degrades when applied to experimental data, as shown in Fig. 3.16. In particular, U-Net enhanced reconstructions of real phantoms exhibit oversharpening and visible artifacts that were not observed when the same network was

applied to simulated data. These effects indicate that the network does not generalize from simulated training data to experimental measurements.

This behavior is a common challenge in machine learning approaches when models are trained exclusively on simulated data. Although the simulations capture the dominant physics of the imaging process, they inevitably differ from the real system in subtle but important ways. These discrepancies may arise from inaccuracies in the modeled magnetic fields, simplified noise assumptions, or idealized descriptions of SPIO magnetization dynamics. When such differences are present, the network may learn features that are specific to the simulated domain and therefore fail to transfer reliably to the experimental setup.

Several strategies could be pursued to improve generalization to real measurements. One approach is to improve the physical accuracy of the simulations used for training. This could include incorporating experimentally measured magnetic field maps rather than relying on Biot–Savart simulations, or fitting simulated fields to measured data to better reflect the true system coil geometry. Additionally, the use of additive Gaussian noise in the simulations is likely an oversimplification of the noise present in the experimental system, and the noise model itself warrants further investigation. In addition, SPIO magnetization models could be improved by using experimentally measured magnetization curves in place of the ideal Langevin model, and by incorporating relaxation effects which are currently absent from the simulations.

Alternative machine learning strategies may also be considered. Rather than attempting full sinogram correction, the network task could be simplified to address a narrower objective, such as denoising or artifact suppression. Another possible direction is to shift from sinogram enhancement to an end-to-end reconstruction approach, in which the network is trained to map noisy pseudo-sinograms directly to reconstructed images. End-to-end approaches are more commonly used across imaging modalities, in part due to

their simplicity. More importantly, integrating a neural network into the middle of a reconstruction pipeline that includes a complex analytical operation such as FBP can be problematic if the network is not explicitly trained to interface with that operation. In such cases, small errors introduced by the network at the sinogram stage may be amplified or propagated in non-trivial ways through the reconstruction process. An end-to-end approach would eliminate this intermediate error propagation by allowing the network to learn the full mapping from measurement to image directly.

Overall, these results demonstrate both the potential and the limitations of machine learning for correcting shift-variant effects in single-sided MPI. While simulation trained networks can substantially improve sinogram and image quality in a controlled setting, achieving reliable performance on experimental data requires further investigation.

CHAPTER FOUR

PROTOTYPE SINGLE-SIDED FFL SCANNER

4.1 Design Goals

The prototype single-sided FFL MPI scanner, first proposed in 2017 [45], was developed with exploratory goals in mind. At the time of its construction, no prior implementations of FFL-based image encoding existed in a single-sided geometry, making this system the first of its kind [82]. The primary objective was to investigate the feasibility and potential of this hardware topology for tomographic imaging and future clinical applications, namely breast cancer applications (Fig. 1.1).

A central motivation for pursuing this design was the challenge of scaling MPI hardware to accommodate human-sized imaging volumes. Single-sided scanners offer a promising solution by confining all hardware components to one side of the imaging region. This open configuration is particularly well-suited for near-surface imaging applications but is often constrained by limited sensitivity.

To address this limitation, the system employs an FFL for spatial encoding. While the original single-sided scanner [41] utilized an FFP, FFL offers theoretical advantages in sensitivity, making it a promising alternative. However, single-sided scanners pose non-trivial challenges in both encoding and image reconstruction. Since FFL had never been implemented in a single-sided MPI system, these challenges required investigation. This prototype was therefore developed to investigate how FFL based imaging could be realized with a single-sided configuration and to identify the practical limitations and design considerations for future implementations.

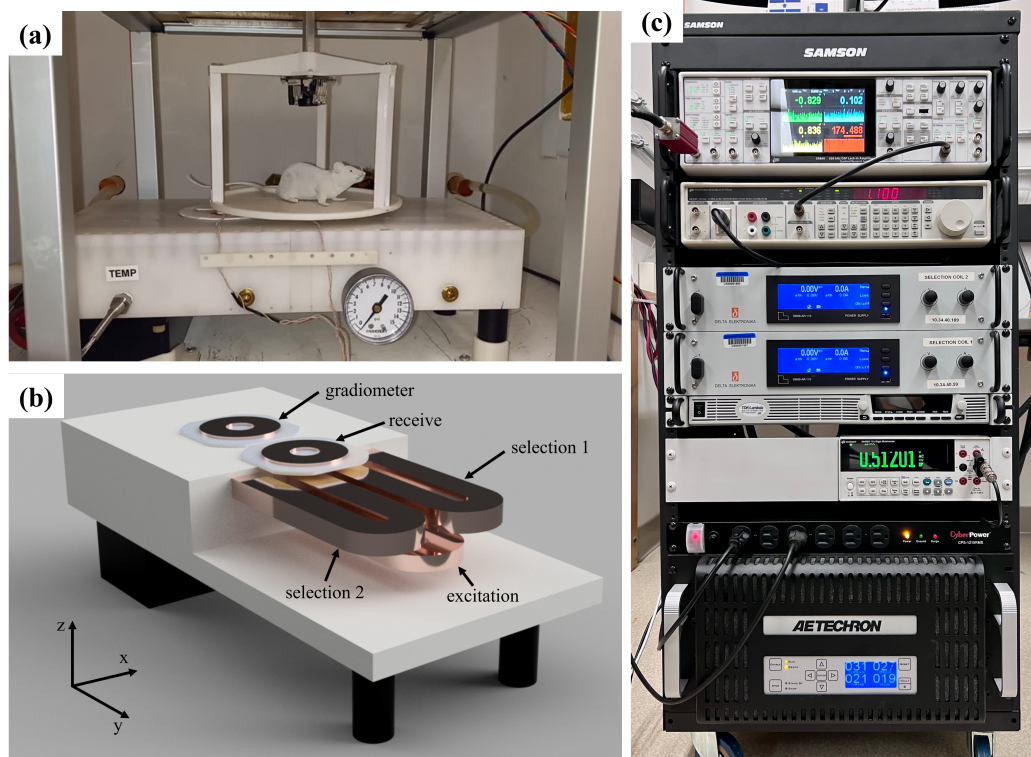


Figure 4.1: **Prototype Single-Sided Scanner Hardware.** (a) Single-sided FFL MPI scanner. A mouse model is placed on the subject table on the surface gradiometer Rx coil. The subject table is capable of automatic rotation and height adjustment. (b) 3D rendering of all coils in a single-sided FFL scanner. (c) The rack with the electronics comprises the excitation and detection chain.

4.2 Scanner Hardware

The single-sided scanner with the electronics rack is shown in Fig. 4.1. The hardware configuration of the scanner encompasses multiple electromagnetic coils, designed according to [45], which both induce and detect signals from an SPIO sample (see Table 6.1). Manufactured by Resonance Research Inc. (Billerica, MA, USA), a water-cooled enclosure houses three racetrack-shaped coils. Among these, the central racetrack coil, designated as the excitation coil, generates the excitation magnetic field at a frequency of 25 kHz. There are two additional racetrack coils known as the selection

Table 4.1: Parameters of the coils.

	Selection Coils	Drive Coil	Receive + Grad
Number of Turns	26×8	26×6	19×2
Wire Cross-Section (mm)	0.82×2	0.82×2	—
Litz Wire Parameters	—	—	AWG 22, 40/38, <i>Type 1</i>
Resistance @ 25 kHz ($m\Omega$)	6150 ± 10	7250 ± 10	1884 ± 10
DC Resistance ($m\Omega$)	144 ± 10	140 ± 10	1233 ± 10
Inductance @ 25 kHz (μH)	360 ± 5	349 ± 5	121 ± 3
Outer Dimensions (cm)	$5 \times 30 \times 1.6$	$5 \times 30 \times 1.2$	$6 \times 13 \times 0.2$

coils, which are located 4 mm beneath the scanner’s surface equidistant from the center. By supplying the selection coils with DC currents, an FFL is created above the scanner’s surface along the y-axis.

Two circular receive (Rx) coils are located on the scanner’s surface. The central Rx coil, positioned directly under the subject imaging table, detects the induced response from the SPIO sample. Another identical circular coil, which is positioned 8.5 cm from the scanner’s center, functions as the gradiometer. The gradiometer subtracts the background signal resulting from the coupling between the excitation coil and the receive coil, eliminating the need for additional filtering. Notably, the surface location of these coils allows for easy replacement with alternative receive and gradiometer configurations [79]. Such adaptability potentially allows for optimization tailored to different pathology. The electrical properties of the receive coil gradiometer pair, as well as those of the selection coils and the excitation coil, are listed in Table 6.1.

4.3 Rotation Table

In the FFL-based MPI, the spatial encoding utilizes a tracer-sensitive line in space. To encode the imaging volume this line is electronically scanned along the x-dimension of

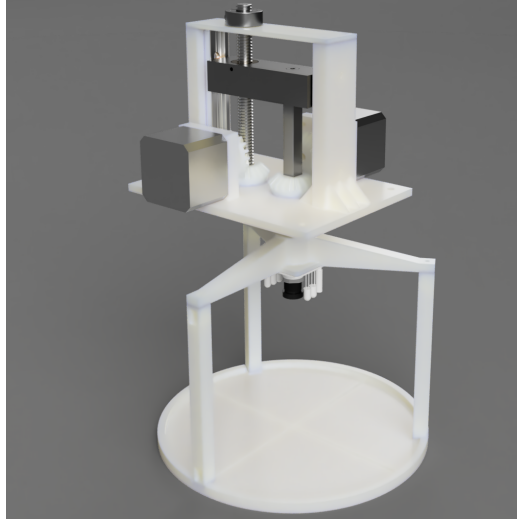


Figure 4.2: **Rotation table diagram.** CAD rendering of custom-built rotation table comprising two stepper motors for the independent rotation and height adjustments.

the scanner, enabling the measurement of a projection of the sample located in the imaging plane. To form an image of the SPIO located in a 2D imaging plane, multiple projections must be acquired at angles ranging from 0° to 180° . Ideally, this would be achieved by rotating the FFL about the subject, requiring mechanical rotation of the scanner. However, the current prototype of the scanner has stationary coils. Therefore, we have built a custom rotational table, which allows for mechanical rotation. Furthermore, for tomographic imaging, multiple 2D slices must be acquired with the FFL located at different heights. In the current setup, this height control is implemented in the rotational table by its mechanical translation along the z-axis.

The rotational table assembly, shown in Fig. 4.2, is capable of rotation and translation of the imaging subject. The table is controlled by two stepper motors, one responsible for rotation, and the other responsible for height control. Notably, to eliminate the interference with weak signals, the stepper motors are turned off during signal acquisition steps. The table's rotational adjustment operates with an angular step size of

1.8°, while the height adjustment employs a step size of 1/100 mm. The dynamic height adjustment facilitates the movement of the phantom within and outside the imaging plane, enabling imaging at multiple depths. The two features of the rotational table allow us to acquire cross-sectional images of the phantom at various depths, achieving a full tomographic imaging capability.

4.4 Signal Acquisition Chain

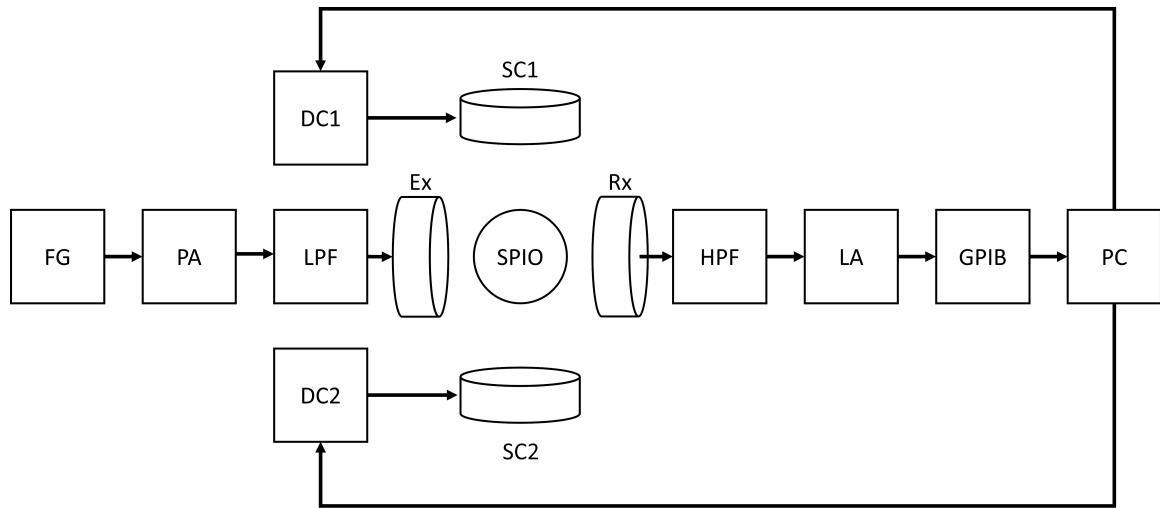


Figure 4.3: **Signal chain diagram:** DC1,2 - DC power supplies, Ex - excitation coil, SC1,2 - selection coils, Rx - receive coil, FG - function generator, PA - power amplifier, LPF - low-pass filter, HPF - high-pass filter, LA - lock-in amplifier, GPIB - general purpose interface bus cable, PC - computer.

Excitation and detection of the SPIO involve a signal chain, as shown in Fig. 4.3. The SPIO is excited at a frequency, $f_1 = 25$ kHz, using an ultra-low distortion function generator DS360 (Stanford Research Systems, Sunnyvale, CA, USA). Amplification of the waveform is achieved by employing a high-power amplifier Techron 7548 (AE Techron, Elkhart, IN, USA).

Further refinement of the excitation waveform is ensured by a custom-made high-power low-pass filter, effectively eliminating undesired higher harmonics with a cut-off frequency of 25 kHz. The filter consists of passive electronic components, including high-power capacitors (Celeem, Israel) and custom-wound Litz wire inductors with an air core, as shown in Fig. 4.4(b). The filter circuit diagram is shown in Fig. 4.4(a), consisting of two inductors ($L_1 = 17 \mu\text{H}$, $L_2 = 64 \mu\text{H}$) and two capacitors ($C_1 = 4 \mu\text{F}$, $C_2 = 1 \mu\text{F}$). The measured inductance of the excitation coil is $L_{\text{excite}} = 358 \mu\text{H}$. In the current iteration, this filter attains an attenuation of 60 dB at the third harmonic. The output waveform, with an amplitude of 6.8 A, is then supplied to the excitation coil, generating an AC magnetic field.

In response to the applied excitation field, the SPIO exhibits non-linear behavior, responding with odd harmonics of the applied frequency. Detection is focused on a single frequency at the third harmonic, $3f_1 = 75 \text{ kHz}$, as the third harmonic exhibits the largest amplitude, besides the base harmonic. The higher harmonics can also be detected in parallel by using a multichannel Lock-In amplifier to gain additional information. The signal is detected with the surface receive gradiometer coils (Sec. 4.2) and the 3rd harmonic is filtered and amplified using a Lock-In Amplifier SR830 DPS (Stanford Research Systems, Sunnyvale, CA, USA). The complex signal is recorded with a GPIB card through a custom-written LabView interface developed on the National Instruments platform (Austin, TX, USA). The rack with the electronics is shown in Fig. 4.1(c) not including the computer station and the excitation filter.

4.5 Spatial Encoding

In conventional MPI, encoding is done by scanning the FFP or FFL across the imaging volume using a fast drive AC field. Therefore, the encoding trajectory typically in the Lissajous shape, is encoded with the speed of the drive frequency [83]. In this approach, the size of the FOV is defined by the amplitude of the drive field. To avoid

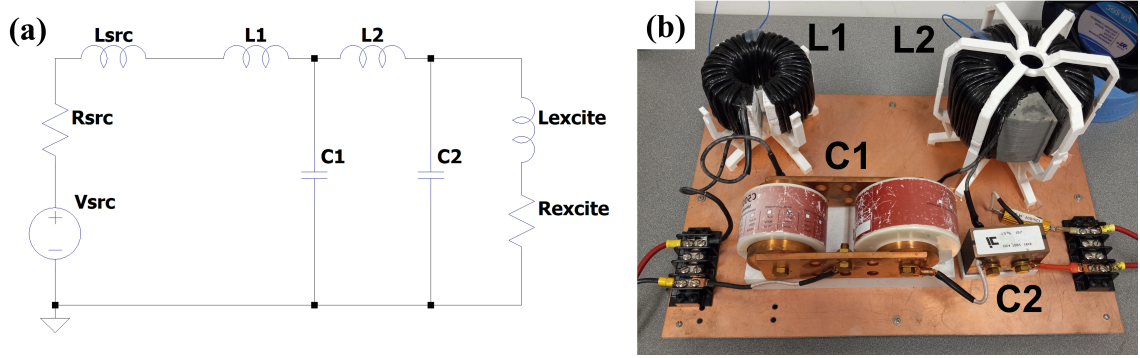


Figure 4.4: **Low-pass excitation filter.** Custom-made low-pass filter for excitation field harmonic rejection. (a) Circuit diagram of the filter, consisting of two inductors ($L_1 = 17 \mu\text{H}$, $L_2 = 64 \mu\text{H}$) and two capacitors ($C_1 = 4 \mu\text{F}$, $C_2 = 1 \mu\text{F}$). (b) Photograph of the realized filter, featuring custom-wound air-core inductors.

applying a large amplitude AC field at high frequency, which is especially important in clinical applications, larger FOVs are typically split into partial (pFOV), and a focus field is used to steer across different pFOVs, known as a multi-patch approach [84], [85].

In our encoding method the object is imaged by electronically advancing the FFL in the imaging plane by creating an asymmetric selection gradient, whereas a relatively weak drive field is applied simultaneously in the direction orthogonal to the plane. Thus, the small oscillation of the FFL along the vertical direction, due to the drive field, does not affect the encoding trajectory. The FOV and scanning rate are not defined by the drive field but by the selection field and the geometry of the selection coils. In this approach, the FOV could be made relatively large by widely separating the coils with arbitrary scanning rate across the sample.

The selection coils are independently controlled by two DC power supplies. When both selection coils are provided with the same current, the FFL is generated in the center of the scanner, at the height $h = 17 \text{ mm}$ above the scanner's surface, as shown in Fig. 2.2. Changing the relative current between the two selection coils causes the FFL to move in

the direction towards the coil with less current. Obtaining a quantitative relationship between the relative current and the position of the FFL allows us to control the coordinates of the FFL exactly. We define a unitless parameter S to quantify the relative current between the two selection coils as

$$S = \frac{I_1 - I_2}{I_1 + I_2}.$$

The x position of the FFL for different S values was measured using a Hall probe. These data were then used to produce a calibration curve between S and the x position of the FFL:

$$S = Ax^3 + Bx,$$

where $A = 8.548 * 10^{-6} \text{mm}^{-3}$ and $B = -0.03318 \text{mm}^{-1}$. These two expressions can be solved for I_1 and I_2 as a function of x , giving the current as a function of the position of the FFL

$$I_1(x) = I_{\text{avg}}[1 + S(x)] = I_{\text{avg}}[1 + Ax^3 + Bx]$$

$$I_2(x) = I_{\text{avg}}[1 - S(x)] = I_{\text{avg}}[1 - Ax^3 - Bx],$$

where I_{avg} is the average current between the two selection coils. The magnitude of the gradient varies linearly with I_{avg} , and varying the average current between the two coils does not affect the position of the FFL.

4.6 Imaging Sequence

To measure a single projection of the subject, the FFL undergoes discrete stepping across the FOV. The AC excitation field is continuously applied to the subject and remains unchanged throughout the entire imaging sequence. All scanner control, data acquisition, and real-time reconstruction were implemented using a custom LabVIEW interface.¹

¹A screenshot of the LabVIEW graphical user interface used for imaging control and reconstruction is provided in Appendix B.6.

At the start of the imaging sequence, both DC power supplies activate, supplying current to the selection coils (see Fig. 4.3) and establishing the FFL at the FOV's edge ($x = -20$ mm). A 1-second delay precedes the recording of the signal measured at the first FFL position. This interval minimizes noise associated with the current transients in the selection coils. The signal is recorded for 80 ms before the FFL is advanced by a variable step size to the next position. At this subsequent position, a 90 ms delay is introduced before signal measurement for current stabilization. This process repeats for a total of 41 FFL positions, ranging from $x = -20$ mm to $x = 20$ mm. This imaging sequence takes 7.9 s to complete and currently, it has been optimized for maximum background reduction. If finer spatial resolution or fast imaging is required, the imaging sequence can be reprogrammed accordingly. Furthermore, background subtraction is implemented through the acquisition of a dedicated background scan, comprising measurements without an SPIO sample. Subsequently, this background signal is subtracted from the overall signal, further reducing background effects in the final image.

An important note about this imaging sequence is that the strength of the magnetic fields varies between FFL positions, this is a direct consequence of the single-sided geometry. Due to this effect to produce the same magnetic field gradient at the edge of the FOV more DC power is required, relative to producing the same gradient at the center of the FOV. Therefore, for constant gradient across the FOV, as limited by the DC power supplies (SM3300, Delta Elektronika, Netherlands), the gradient in the center of the FOV is adjusted to match the edges.

4.6.1 FBP Imaging in the XY Plane

For FBP imaging in the horizontal (XY) plane, the rotational control of the subject table described in Sec. 4.3 was utilized. The FFL was electronically scanned across the x direction of the phantom, ranging from -2 cm to 2 cm, to capture a projection. This is done with a uniform imaging gradient of 0.58 T/m across the FOV, when the FFL is

located in the center of the FOV this is achieved by supplying each selection coil with 55 A DC. This corresponds to an average electrical power of 1500 W in the scanner. Subsequently, the sample was mechanically rotated, and the process was repeated to obtain projections at various angles. This procedure was conducted for 20 angles spanning from 0° to 180° , creating a sinogram of the imaging subject. Each projection is acquired by averaging four individual projections, as described in Sec. 4.6, corresponding to a measurement time of 32 s per averaged projection. To acquire the full set of projections at 20 different angles the total acquisition time is 10 min and 40 s. A 2D image reconstruction was performed through the FBP method on the measured sinogram with the Hann filter. Due to utilizing FBP for reconstruction a homogeneous gradient across the FOV must be used to avoid imaging artifacts. Post-processing of the image was done through deconvolution with a simulated PSF, using the Lucy-Richardson algorithm. The PSF was simulated using the same parameters as used in imaging, further details of the simulations can be found in [86]. The simulation of the PSF involved applying the identical current sequences to the excitation and selection coils as those used during the actual imaging process. This ensured that the simulated PSF accurately captured the specific magnetic field dynamics and gradients experienced by the particles within the scanner during image acquisition. Additionally, the PSF was generated by simulating the response of a point source located at the center of the imaging FOV.

4.6.2 2D Projection Imaging in the XZ Plane

In addition to 2D imaging in the horizontal (XY) plane, our scanner is capable of 2D imaging in the vertical plane (XZ). Imaging in the vertical plane is a non-tomographic 2D imaging technique. The image produced by this method is a 2D projection of the subject similar to that of X-ray. For this imaging method, the FFL is electronically scanned across x dimension to obtain a projection of the subject at a single height, this is done with a central imaging gradient of 0.84 T/m. This gradient is achieved by supplying

each selection coil with a DC current of 80 A, corresponding to an average power of 3000 W in the scanner. The gradient in the center of the FOV is larger when compared to FBP imaging in the horizontal plane. Next, the subject is mechanically raised by 0.5 mm, using the subject table described in Sec. 4.3, and the scan is repeated. Repeating this process for several height positions allows us to obtain a 2D projection image of the subject in the vertical plane. No special reconstruction is used for this method besides background subtraction, which is why a homogeneous gradient is not required across the FOV.

4.6.3 3D Tomographic Imaging

The scanner is capable of performing 3D tomographic imaging by utilizing both functionalities of the sample table, rotation and height adjustment of the subject. For 3D tomographic imaging, we perform FBP imaging of the sample in a horizontal plane at a fixed height followed by another slice acquisition by advancing the sample in the z direction of the scanner. This allows us to obtain XY cross-sections of the phantom at different heights, each cross-section takes 5 min 20 s to obtain the image. These cross-sectional measurements are obtained twice as fast when compared to the single-slice studies, owing to a reduced amount of averaging. The decision to reduce averaging was justified by the sufficient image quality achieved with this modified approach.

The total FOV in this imaging mode is $4\text{ cm} \times 4\text{ cm} \times 1\text{ cm}$. The acquired data form a 3D matrix comprising multiple imaging planes of the subject, with each plane representing a 2D FBP image. To visualize this 3D data, individual XY slices can be displayed. Alternatively, Maximum Intensity Projection (MIP) can be utilized to render 3D volume and obtain slices of it in the XZ plane.

4.7 Results

The following section presents imaging results from a series of phantoms designed to demonstrate the capabilities of the scanner.

4.7.1 Dual-Plane Imaging of Rod Phantoms

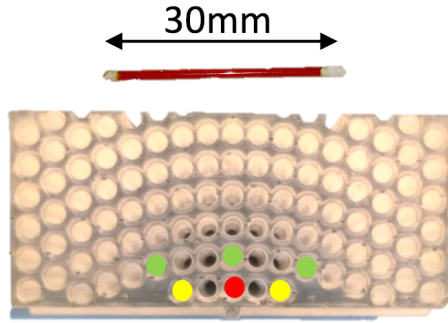


Figure 4.5: **Glass rod phantom holder.** Glass rod of length 30 mm filled with Synomag-D, with a 3D printed holder. The holder is designed to position multiple rods at different positions, indicated by color dots, in the XZ plane above the surface of the scanner.

To study the dual imaging capability of the scanner in both the XY and XZ planes we imaged a series of rod phantoms. These phantoms consist of glass rods, with a length of 30 mm and a diameter of 1 mm, filled with undiluted Synomag-D SPIO. A 3D resin-printed structure was made to hold the rods at different separations and heights above the scanner's surface. In XZ plane imaging the phantoms were located along the y direction of the scanner, making them parallel to the direction of the FFL. The rods and their holder are shown in Fig. 4.5.

Fig. 4.6 shows experimentally obtained images of glass rod phantoms captured in the XY and XZ planes. Various configurations of glass rods were examined in the XZ plane, utilizing a central imaging gradient of 0.84 T/m and a excitation field strength of 1.6 mT at the scanner's surface. One notable phantom in this study, as shown in Fig. 4.6(a), is

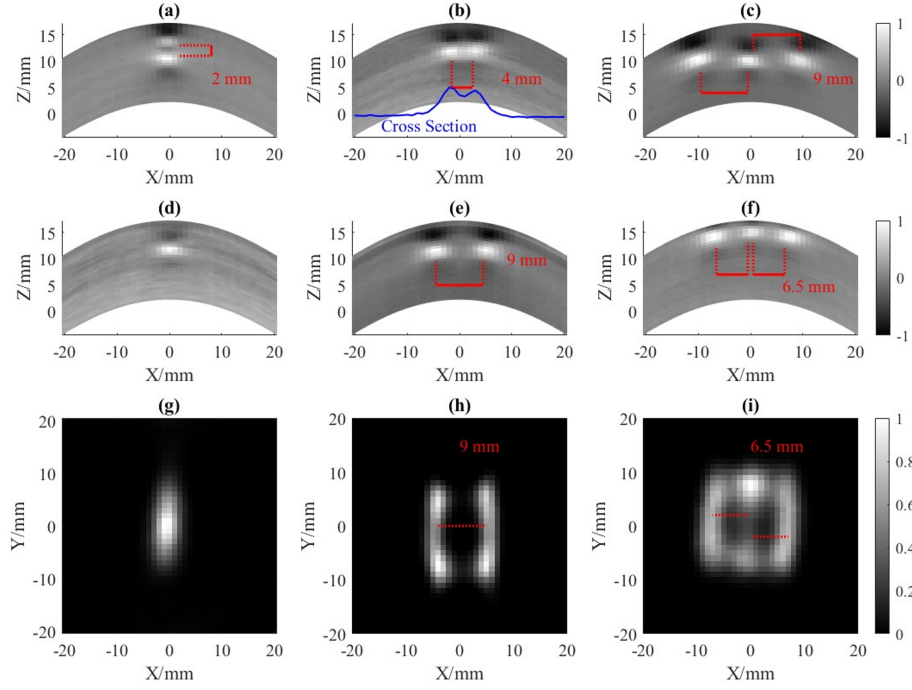


Figure 4.6: **MPI images of various rod phantoms.** (a) Two rods separated by 2 mm (edge to edge) in the z-direction. (b) Two rods separated by 4 mm (edge to edge) in the x direction, with cross-section at the height of rods. (c) Three rods separated in x by 9 mm. (d) Single SPIO-filled rod located in the center of the FOV. (e) Two SPIO-filled rods separated by 9 mm (edge to edge). (f) Three SPIO-filled rods separated by 6.5 mm (edge to edge). (g) FBP cross-section in the XY plane of the same phantom in (d). (h) FBP cross-section in the XY plane of the same phantom in (e). (i) FBP cross-section in the XY plane of the same phantom in (f).

the z separation phantom. This phantom comprises two glass rods separated by 2 mm edge to edge, demonstrating the scanner's spatial resolution of 2 mm along the z-direction.

Additionally, we imaged a rod phantom separated along the x-axis in the XZ plane, featuring two rods separated by 4 mm edge to edge. The resulting image, displayed in Fig. 4.6(b), validates a spatial resolution of 4 mm along the x-direction. These results demonstrate the spatial resolution capabilities of the scanner in its XZ plane imaging mode.

In addition to imaging phantoms in the XZ plane (depicted in Fig. 4.6(a-f)), we extended investigations to the XY plane using the FBP imaging technique, as illustrated in Fig. 4.6(g-h). Notably, when imaging in the XY plane, the gradient is presently constrained to a maximum of 0.58 T/m at the center of the scanner (Sec. 4.6.1), while utilizing the same excitation field strength. Despite the existing limitation in gradient strength along this plane, the phantom showcased in Fig. 4.6(f), comprising three rods separated in the x direction by 6.5 mm edge to edge, demonstrates a spatial resolution of 6.5 mm. It is worth noting that in the XY plane, the spatial resolution is uniform in both the x and y directions. This imaging analysis provides insight into the current capabilities of the scanner, particularly emphasizing its performance in the XY plane under the specified gradient constraints.

4.7.2 Imaging of an Anatomical Mouse Phantom

A mouse phantom (Bioemtech, Greece) was used as a subject to demonstrate the potential for preclinical applications. The phantom replicates the size, shape, and spatial arrangement of typical mouse organs through various cavities as shown in Fig. 4.7. Three distinct configurations of this phantom were imaged, each featuring two distinct cavities filled with undiluted Synomag-D 70 nm (Micromod, Germany) SPIO. The first configuration entails both kidneys filled with SPIO, each possessing a volume of 352 mm^3 . The second configuration comprises the bladder and a "tumor", exhibiting volumes of 294 mm^3 and 204 mm^3 respectively. The third configuration incorporates a liver volume and heart volume, with volumes measuring 1164 mm^3 and 277 mm^3 respectively.

The FBP images, displayed in Fig. 4.7, showcase all three configurations of the mouse phantom captured in the XY plane with a magnetic field gradient of 0.58 T/m and a excitation field amplitude of 1.6 mT at the scanner's surface. In the imaging process, 20 projections of the phantom were acquired at varying angles, with each projection

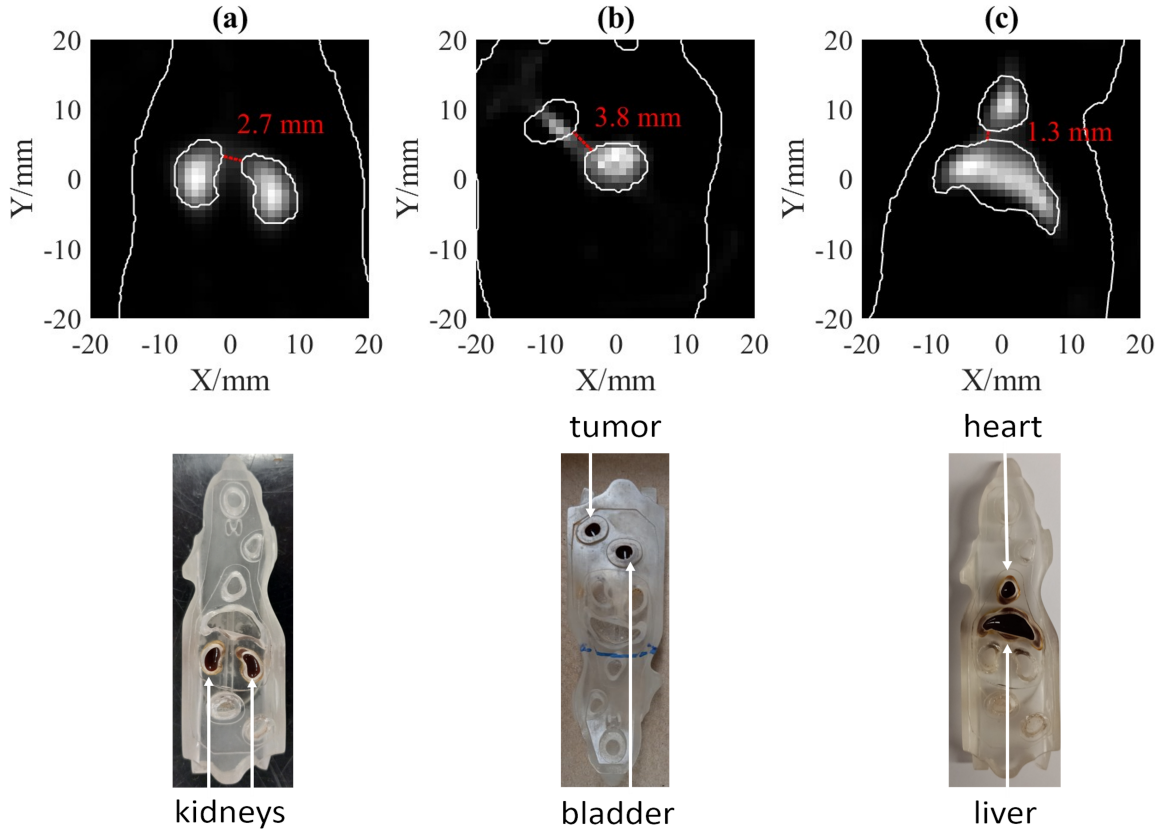


Figure 4.7: **Mouse phantom imaging.** (a) XY cross-section of mouse phantom with both kidneys filled with SPIO. (b) XY cross-section of mouse phantom with tumor and bladder filled with SPIO. (d) XY cross-section of mouse phantom with heart and liver filled with SPIO.

comprising 41 different FFL positions and a step size of 1 mm. Employing MATLAB (Natick, MA, USA) built-in Lucy-Richardson algorithm for deconvolution, we observed optimal image quality for the kidney phantom at $iter = 10$, $dampar = 0$, and $weight = 1$, while the other phantoms exhibited superior quality at $iter = 20$, $dampar = 0$, and $weight = 1$.

In all three configurations of the mouse phantom, the organs are fully resolvable, retaining most geometrical features. Particularly noteworthy is the ability to distinguish

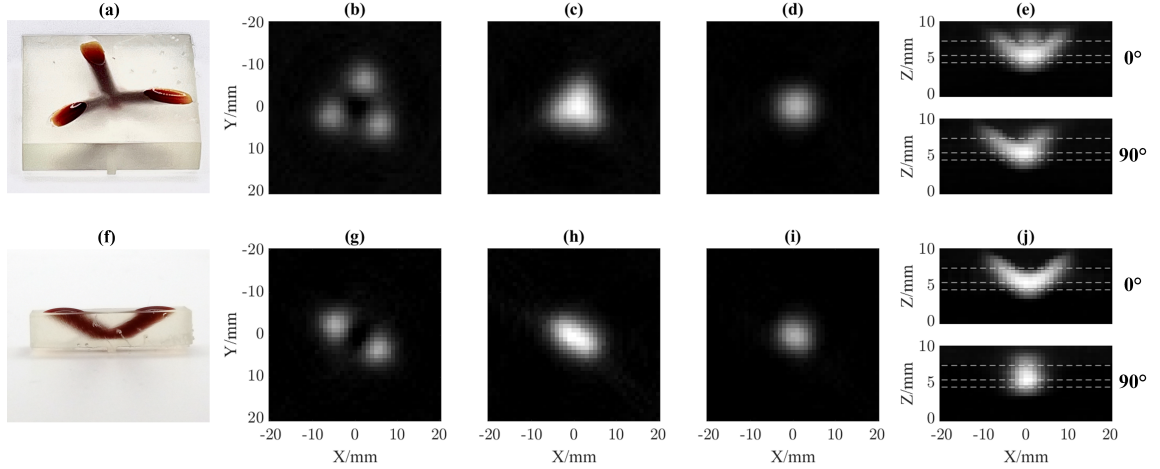


Figure 4.8: Tripod phantom 3D imaging. (a) Photo of the Tripod Phantom, showcasing a resin-printed structure with three rods converging to a single point, filled with undiluted Synomag-D SPIO. (b,c,d) FBP images in the XY plane of the tripod phantom located at different heights. (e) MIP images in the XZ plane of the phantom at two different angles 90° apart from each other. (f) Photo of the Two-Vessel Phantom, featuring a resin-printed structure filled with undiluted Synomag-D SPIO. (g,h,i) FBP images in the XY plane of the two-leg phantom located at different heights. (j) MIP images in the XZ plane of the phantom at two different angles 90° apart from each other.

volumes in the heart and liver configurations, despite their features being separated by a mere 1.3 mm. The imaging of this phantom serves as a testament to the scanner's current spatial resolution, demonstrating its capability to spatially distinguish mouse organs and detect tumors within a mouse.

4.7.3 Three Dimensional Imaging of a Tripod Phantom

For tomographic imaging, we utilized two 3D-printed phantoms mimicking dual and three blood vessel manifolds. The two-vessel 2D structure in the vertical plane consists of two rods converging at a single point. The tripod phantom is a 3D structure of three vessels converging at a single point. The experimental dataset comprises images of the two-vessel and tripod phantoms at 20 different heights, with a height step of 0.5 mm,

resulting in a total height range of 1 cm. Each height position required an imaging time of 5 minutes 20 seconds, with a cumulative imaging time of 1 hour 47 minutes.

The individual reconstruction of each XY slice was performed using the FBP algorithm with a Hann filter. The resulting images are depicted in Fig. 4.8. For both phantoms two XY cross-sections are featured within the dataset: one clearly delineating two and three vessels and the other illustrating the vessels merging into a single point. Additionally, the figure includes XZ plane images of the phantoms, presenting cross-sections that are Maximum Intensity Projection (MIP) images of the 3D data. Two distinct XZ projections are showcased: one at an angle of 0° and another at an angle of 90° . From these projections all spatial features of the phantoms are visualized, demonstrating the scanner's capability of imaging complex 3D structures.

4.7.4 Imaging Artificial Tumors in an Anatomical Breast Phantom

To demonstrate the utility of the single-sided MPI scanner in accommodating the realistic human breast, we acquired an anatomical medical training breast phantom (SynDaver, FL, USA). While its complex tissue structure can be imaged with conventional imaging modalities such as ultrasound, MPI does not directly image the tissue. Therefore, artificial SPIO-labeled tumors were implanted into the phantom. Specifically, two small glass bulbs (18 μ l each) were filled with undiluted Synomag-D 50 nm (10 mg/ml) SPIOs to serve as artificial tumors. This constitutes an adequate tumor model for MPI because the modality depends only on the spatial distribution of tracer particles rather than the mechanical properties of the tissue, and tumors naturally accumulate SPIO through the enhanced permeability and retention (EPR) effect. These "tumors" were implanted 7 mm beneath the skin of the phantom and positioned at the 12 and 1 o'clock locations, 39 mm and 20 mm from the nipple and spaced 16 mm apart. The breast phantom with the implanted tumors can be seen in Fig. 4.9(d). For imaging, the

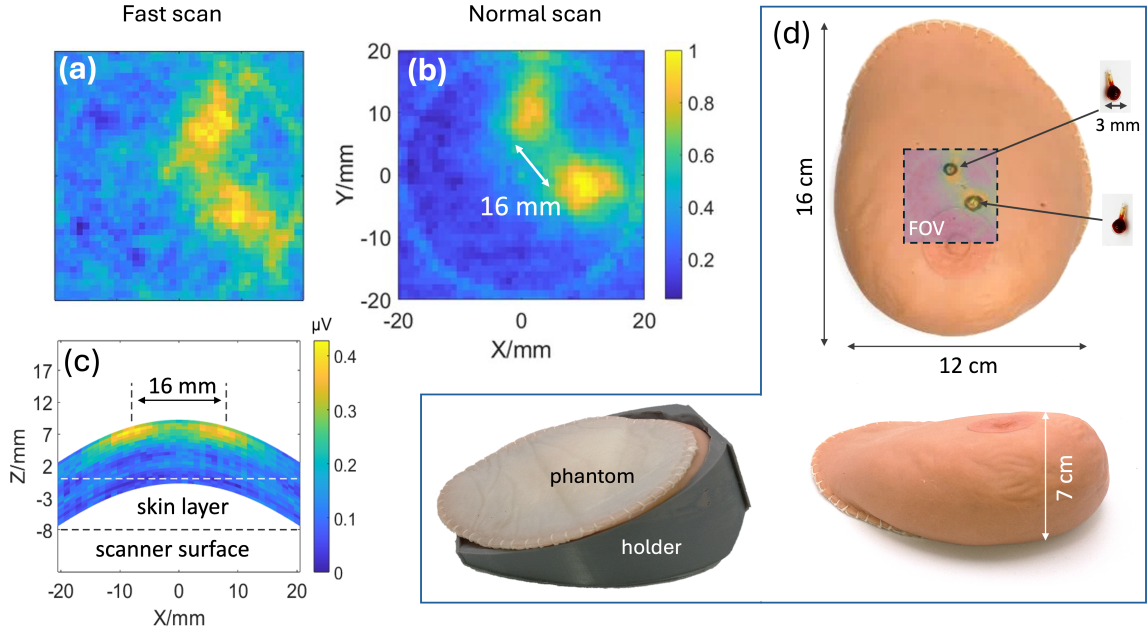


Figure 4.9: **Anatomical breast phantom with MPI images.** (a) MPI image of artificial SPIO tumors from a fast scan (100 s) in a coronal plane. (b) High SNR MPI image in a coronal plane of tumors from a slow (10 min) scan. (c) MPI image of breast tumor model in axial plane (total acquisition time 10.5 min). (d) Anatomical breast phantom with labeled dimensions in two orthogonal views. Two 18 μl glass bulb SPIO (Synomag-D 50 nm) tumors are embedded in the breast phantom under the skin, placement shown as black circles, and the respective imaging FOV indicated as a square. Bottom-left: 3D printed holder for the breast phantom with the breast phantom placed inside in a prone position, used for consistent positioning of a phantom in the scanner.

phantom was secured in a custom 3D-printed holder, oriented nipple-side down, and positioned on a rotation table above the scanner.

To image the artificial tumors in the breast phantom imaging was done in both the XY and XZ planes. For imaging in the XY plane two separate acquisition times were used. A short duration scan (100 s) was used to demonstrate that viable imaging can be performed under clinically practical time frames, and a longer scan (10 min) was performed to obtain a high SNR image. For imaging in the XZ plane a singular scan was taken of the subject with an imaging time of 10.5 min.

The resulting images are shown in Fig. 4.9. The coronal image reveals two distinct hotspots corresponding to the tumor models, with a measured separation of 16 mm, consistent with their known implant location. The longer duration scan (Fig. 4.9(b)) provides high contrast images with clearly resolved tumors, while the shorter duration scan (Fig. 4.9(a)), though noisier, still allows both tumors to be distinctly resolved. The axial projection further confirms the lateral separation of the tumors and measures their depth of 7 mm below the surface of the skin. In both views, the tumors are clearly resolved with high contrast and no visible background signal from the surrounding tissue. This tracer-specific contrast represents a fundamental advantage of MPI over conventional modalities such as ultrasound, which generate a background signal from all tissue rather than targeted regions.

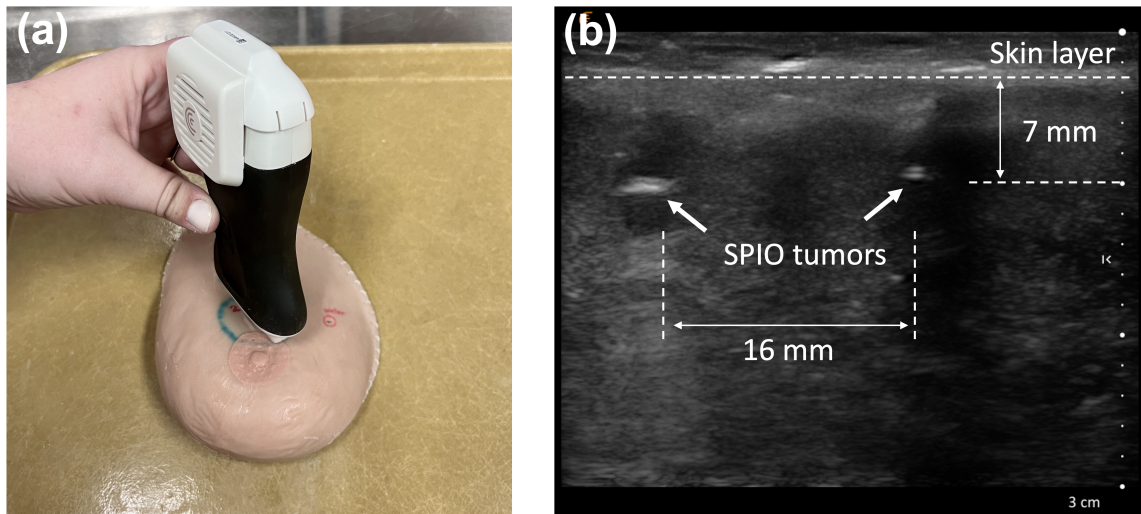


Figure 4.10: **Ultrasound validation of SPIO tumor positions in anatomical breast phantom.** (a) Scanning with a handheld ultrasound imaging probe positioned on the top skin layer of the breast phantom. (b) Ultrasound image in axial plane showing two SPIO tumors located 7 mm beneath the phantom's surface, with a center-to-center separation of 16 mm. Dashed lines indicate the skin layer and horizontal positions of SPIO tumors.

For reference to MPI imaging, ultrasound imaging was performed using a Clarius L7HD3 linear array (Clarius Mobile Health, Vancouver, Canada), and the position of the tumors were measured. The ultrasound scan revealed the two artificial "tumors", due to scattering of acoustic waves on glass boundaries of tumors, with the bottom lateral edge of the transducer 1 cm from the nipple and in an approximately radial position. The resulting measurements from the ultrasound images confirmed that the artificial tumors were located 7 mm beneath the breast phantom's skin and were separated by 16 mm, as shown in Fig. 4.10(b). It is important to note that these glass bulb "tumors" are not an adequate tumor model for ultrasound, since the modality depends upon the tissue properties, and glass is not analogous to tumor tissue in terms of its physical characteristics. Consequently, the ultrasound images serve only to coregister the positions of the implanted glass bulb "tumors" and do not represent a demonstration of ultrasound's ability to resolve small tumor masses.

Due to the small size of the SPIO tumor masses, they were difficult to visualize fully in the ultrasound images. However, the bright reflection off the glass bulb confirms the presence of the SPIO tumors. A dark artifact was observed beneath one of the tumors, likely caused by acoustic shadowing, which can occur when ultrasound waves are attenuated or reflected by dense or highly absorptive materials. Additionally, the inherent background signal from the phantom's tissue-mimicking material reduced the contrast between the SPIO tumors and the surrounding medium. While this limits the ability of ultrasound to directly visualize the tracer masses, it provides anatomical context that may be valuable when correlating ultrasound with MPI imaging.

4.8 Conclusion

This chapter presented the design, implementation, and experimental performance of the original prototype single-sided FFL MPI scanner [45], [58]. Despite the challenges associated with an FFL single-sided geometry, this implementation of the scanner

demonstrated for the first time full 3D tomographic imaging capability (Sec. 4.7.3). Two distinct imaging modes were realized: XY FBP imaging, in which the sample is mechanically rotated in the imaging plane to acquire multiple projections, and XZ plane projection imaging, in which the sample is translated vertically to acquire projections at different heights. A series of phantom experiments were performed to characterize the performance of this implementation of the scanner and to demonstrate the potential of this scanner topology for clinically motivated breast imaging applications.

The spatial resolution of the system was evaluated through imaging of rod phantoms (Sec. 4.7.1). These measurements demonstrated a maximum spatial resolution of 2 mm along the z-axis and up to 4 mm along the x-axis in XZ projection imaging. In the horizontal plane, XY FBP imaging of rod phantoms yielded a spatial resolution of at least 6.5 mm. In addition, the scanner successfully resolved anatomical features in a mouse organ phantom with separations as small as 1.3 mm (Fig. 4.7). Together these results demonstrate clinically relevant spatial resolution, and demonstrate the scanner's ability to image biological organ geometries.

A major result of this chapter was the imaging of artificial tumors implanted in an anatomical breast phantom (Sec. 4.7.4). The breast phantom demonstrates the unique advantage of the single-sided scanner topology for its ability to accommodate realistic human-sized anatomy, a unique feature of our scanner. The implanted SPIO tumor models were clearly resolved in both coronal and axial imaging planes, with measured separation and depth consistent with their known placement. These results demonstrate the feasibility of near-surface tumor detection using a single-sided FFL MPI scanner and motivate further development of this approach for breast imaging applications.

Together, these demonstrated imaging capabilities represent significant progress in the development of a single-sided MPI scanner. The success of this implementation led to its adoption as "the standard" design for subsequent single-sided MPI developments [87].

Despite this success, this implementation still suffered from challenges historically associated with single-sided MPI, most notably limited and spatially inhomogeneous sensitivity. These challenges restricted the usable FOV, and restricted imaging studies to phantoms rather than biological subjects. To address these limitations, multiple hardware and software upgrades were implemented, which are discussed in detail in Chapter 5.

CHAPTER FIVE

ORGAN-SPECIFIC SINGLE-SIDED FFL SCANNER

5.1 Design Goals

The design goals of this version of the scanner are the following [88]. The original prototype of the scanner suffered from limited imaging sensitivity. Not only limited imaging sensitivity but non-uniform imaging sensitivity as well. It also suffered from a non-linear FFL trajectory leading to both limited FOV, penetration depth, and imaging artifacts.

To address all these limitations a new external excitation coil was developed. This coil surrounds the imaging volume providing superior field strength and homogeneity. In addition to this external excitation coil this implementation of the scanner can repurpose the previous internal excitation coil as an additional selection coil, utilizing the algorithm in Sec. 5.5.

5.2 Hardware Overview

The single-sided MPI scanner used in this study is a significantly upgraded version of the system previously described in [58]. The current system comprises six electromagnetic coils: three embedded racetrack-shaped selection coils housed within a custom water-cooled enclosure, and three surface-mounted coils including the receive coil, cancellation gradiometer, and a newly added surface excitation coil.

The two uppermost embedded racetrack coils function as primary selection coils, producing a static magnetic field gradient that creates a field-free line (FFL) oriented along the y-axis. A third embedded racetrack coil, originally utilized as an excitation coil [58], is now repurposed as an auxiliary selection coil. This modification introduces an additional degree of freedom, enabling full control over the FFL position in the XZ plane.

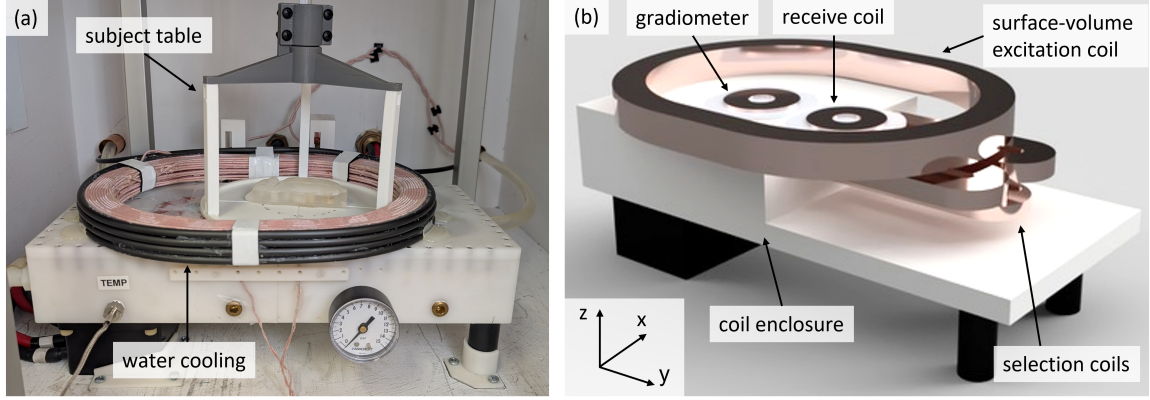


Figure 5.1: **Organ-Specific Single-Sided Scanner Hardware.** (a) Photograph of the single-sided FFL MPI scanner. Visible components include the newly added surface excitation coil, the surface-mounted gradiometer, the water-cooled enclosure housing the embedded selection coils, the 185 mm subject table, and a mouse phantom positioned on the rotating sample stage. (b) 3D rendering of the scanner showing the three embedded racetrack-shaped selection coils, the surface-mounted receive and gradiometer coils, and the surface excitation coil.

As a result, the system can maintain a flat FFL trajectory at a fixed height of 17 mm above the scanner surface and extend the usable field of view laterally.

Signal detection is performed by a circular receive coil located at the center of the scanner surface. A second, laterally offset circular coil functions as a cancellation gradiometer to suppress background signal from the excitation field [79]. Both coils are easily replaceable, enabling flexible adaptation for different anatomical targets.

New to this iteration of the system is the surface excitation coil, which generates a 25 kHz AC magnetic field to drive SPIO oscillations. This racetrack-shaped coil surrounds the 185 mm subject table shown in Fig. 5.1(a), delivering stronger and more homogeneous excitation across the imaging field of view compared to the original embedded excitation coil. Its geometry also provides improved coupling to the surface-mounted receive and gradiometer coils, further enhancing signal quality [79].

5.3 Surface-Volume Excitation Coil

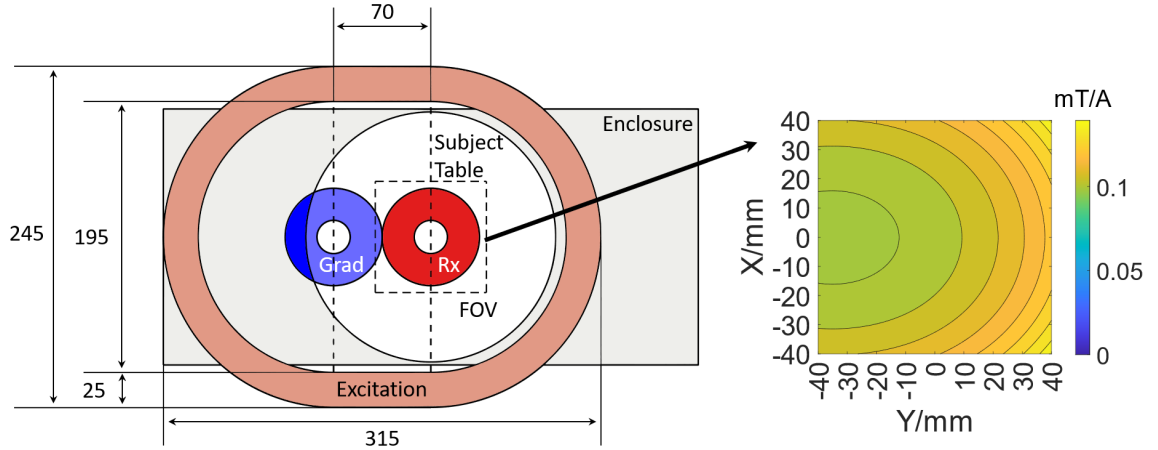


Figure 5.2: **Schematic of the surface excitation coil.** The coil has a racetrack geometry with outer dimensions of 315 mm $\times$ 245 mm and a winding width of 25 mm. The inner diameter measures 195 mm in height and 70 mm in width, providing clearance for the 185 mm subject table. Markers indicate positions of geometric symmetry defined by the coil layout, where the receive and gradiometer coils are placed. This symmetry results in nearly identical coupling to the excitation field and enables improved gradiometric cancellation.

A major hardware upgrade in the current scanner design is the addition of a new surface excitation coil, which replaces the embedded excitation coil used in prior work [58]. The new geometry improves excitation field strength and uniformity in the imaging FOV while maintaining compatibility with the scanner's surface receive and gradiometer coils [79].

The coil features a racetrack geometry with an inner diameter of 195 mm in height and 70 mm in width, sized to fit the subject table. The overall outer dimensions are 315 mm in length and 245 mm in width, and the coil has a total height of 28.5 mm. It was

custom fabricated by winding 14 AWG Litz wire around a 3D printed PLA former, and glued together using a clear adhesive. The coil consists of eight layers with ten turns per layer. The layers are connected in a series-parallel configuration: four sets of two layers are connected in series, and those four series elements are then connected in parallel. This configuration reduces the total inductance and impedance, supporting integration with the custom excitation filter. The measured electrical properties at 25 kHz are 141.1 μH inductance and 417 $\text{m}\Omega$ resistance, as determined using an LCR meter.

The coil's geometry enables symmetric placement of the receive and gradiometer coils relative to the excitation field, as shown in Fig. 5.2. This spatial symmetry results in nearly identical coupling to both receive channels, substantially improving gradiometric cancellation from 41 dB in the previous design to 55 dB in the current configuration [79]. Additionally, mounting the coil directly on the scanner surface reduces the distance to the imaging plane, providing a more uniform excitation field in the imaging plane of 17 mm, with a magnetic field per unit current of 0.102 mT/A in the center of the FOV.

Due to its improved electrical properties, the new surface coil is able to achieve higher and more stable currents. In previous systems, excitation was limited to 5 A_{rms} , producing 0.58 mT_{rms} at a height of 17 mm. The new coil is able to achieve a stable current at 29 A_{rms} , generating 2.96 mT_{rms} representing a tenfold increase in excitation field strength. These improvements directly contribute to higher imaging sensitivity.

5.4 Excitation Filter

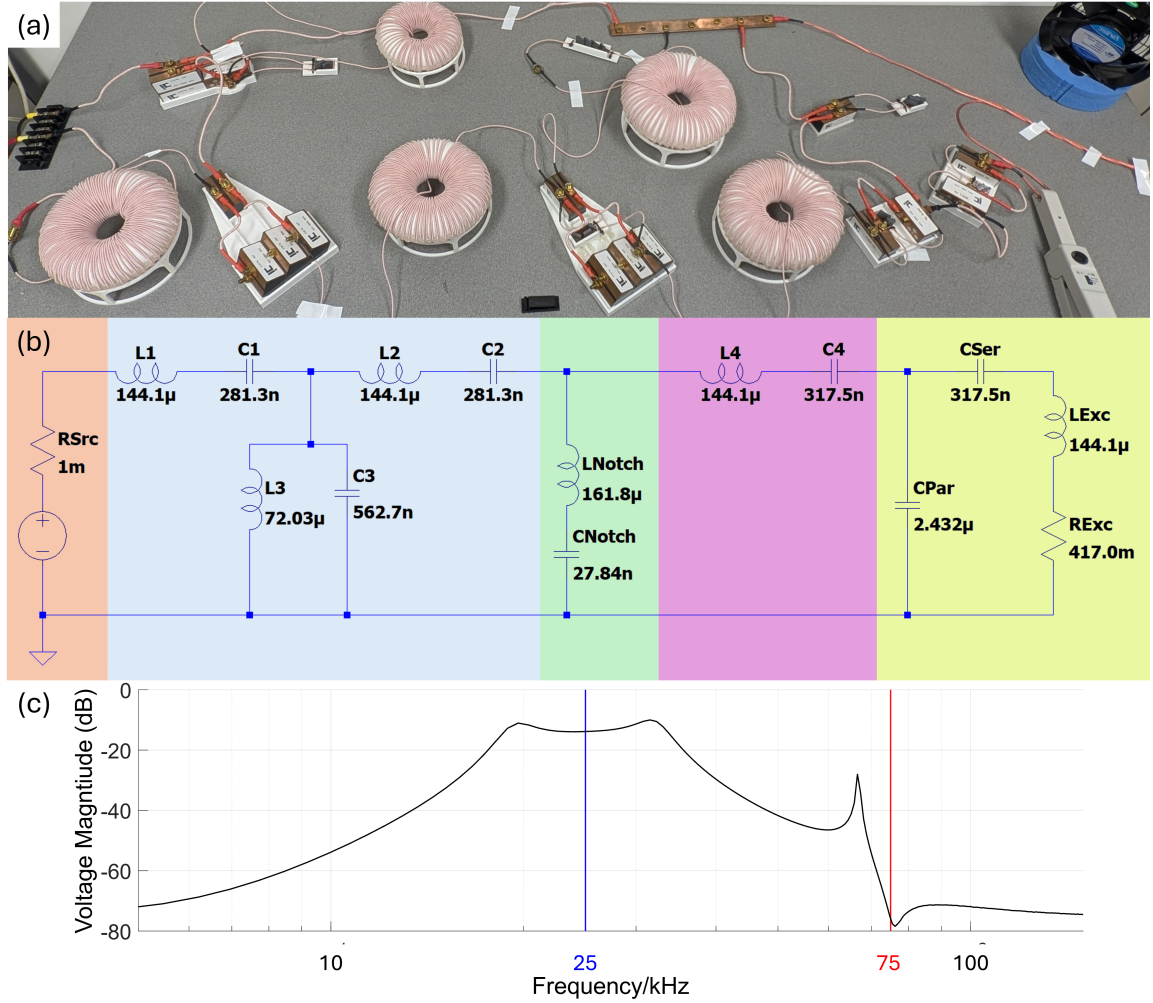


Figure 5.3: **Photograph and schematic of the multi-stage resonant filter for the surface-volume excitation coil.** (a) Photograph of the multi-stage resonant filter. (b) Schematic of the multi-stage resonant filter for our excitation coil. The circuit is divided into five functional stages, highlighted by background color. Red: AE Techron 7548 power amplifier. Blue: Double-tuned bandpass filter with a shunt resonator, centered at 25 kHz. Green: Notch filter tuned to suppress the third harmonic at 75 kHz. Purple: Inductor capacitor pair tuned to 25 kHz to optimize power transfer to the excitation coil. Yellow: Excitation coil with resonance capacitors for impedance matching. (c) Experimentally measured voltage transfer function of the filter, acquired using a network analyzer.

A custom excitation filter was developed to deliver high-amplitude, harmonically pure (25 kHz), and thermally stable current to the surface excitation coil. The design is based on a topology proposed in [89], which was optimized specifically for thermal stability. This is a major concern in MPI, as thermal fluctuations in the excitation current can lead to baseline drift and inconsistencies in the background signal. These effects are particularly problematic in systems that rely on background subtraction during reconstruction, a common practice in MPI that assumes a temporally stable background. Even small instabilities in excitation can introduce subtraction errors that degrade image quality [89].

The filter circuit, shown in Fig. 5.3, consists of a sequence of LC stages tuned primarily to the 25 kHz excitation frequency. Its roll is to pass the fundamental frequency while suppressing higher harmonics that would otherwise distort the excitation waveform. The architecture combines series and parallel resonant components: series LC stages provide a low-impedance path for the primary frequency, while parallel stages shunt higher harmonics to ground. A single notch filter tuned to 75 kHz is included to suppress the third harmonic explicitly. Following the approach described in [89], the filter is designed with decreasing impedance along its length. The early stages operate in a voltage-dominant regime, reducing current and thus limiting heating in the early filter elements. Toward the end of the filter, the impedance drops, shifting power into the current-dominant regime needed to generate the magnetic field in the excitation coil.

All inductors were hand-wound using Litz wire to reduce AC resistance and were constructed on air-core formers to avoid the generation of unwanted higher harmonics. High-power capacitors (Celem, Israel) were used in each resonant stage, and were precision-tuned with parallel film capacitors to achieve final capacitance values within 0.1% of the target value. The filter was tuned to match the impedance of our excitation coil, which has a measured inductance of 141.1 μH and resistance of 417 $\text{m}\Omega$ at 25 kHz.

This inductance was deliberately chosen to ensure the feasibility of constructing the resonant filter elements, particularly the custom inductors, which must have comparable inductance to the load. Higher inductance would require more turns of wire and physically larger inductors, making the filter more difficult to construct and less thermally efficient. In previous scanner iterations, the maximum excitation current was limited to $5 A_{\text{rms}}$ due to heating in the filter. In contrast, the present design supports stable operation at $29 A_{\text{rms}}$, yielding an excitation field of $2.96 \text{ mT}_{\text{rms}}$ at a height of 17 mm above the scanner surface. The thermal limitation has now shifted to the excitation coil itself, marking a substantial improvement in system performance.

5.5 FFL Generation and Control

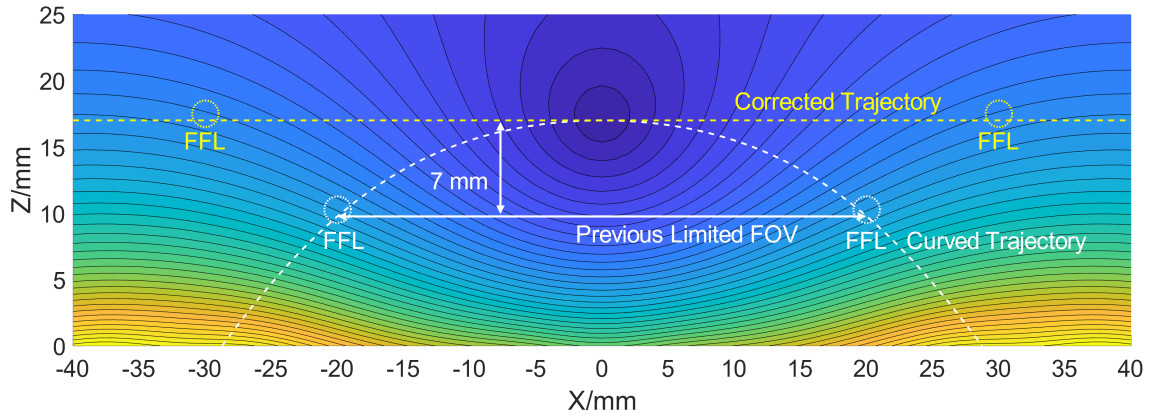


Figure 5.4: **FFL trajectory correction algorithm.** Magnetic field profile with lines showing the trajectory of the FFL with and without the correction algorithm.

Precise electronic control of the FFR is critical for MPI, as it defines the region of signal sensitivity and enables spatial encoding. In closed-bore MPI systems, the FFR is typically formed by symmetric selection fields with well-understood behavior. In contrast,

single-sided topologies produce inherently inhomogeneous magnetic fields, making it nontrivial to position the FFL at arbitrary locations or with consistent gradient strength. This lack of linearity complicates both image acquisition and reconstruction. To address this, we developed an algorithm that computes the currents required to place the FFL at any desired location, with a specified gradient magnitude. This approach enables full electronic control of both FFL position and resolution across the FOV, and forms the basis for our imaging protocol.

Our system employs three independent selection coils, thus the total magnetic field they generate is given by the superposition of each:

$$\mathbf{B}_{\text{tot}}(x, z) = I_1 \mathbf{P}_1(x, z) + I_2 \mathbf{P}_2(x, z) + I_3 \mathbf{P}_3(x, z)$$

Here, $\mathbf{P}_i(x, z)$ denotes the magnetic field produced from selection coil i per unit current at the central XZ plane, which we measured experimentally. Because the scanner generates an FFL along the y-axis and the selection coils are much longer than the imaging region, we assume translational invariance in the y-direction. This simplifies the 3D field problem (x, y, z) to a 2D plane in (x, z) , allowing a slice-wise approach to field control.

To place the FFL at a specific position $\mathbf{r}_{\text{FFL}} = (x_{\text{FFL}}, z_{\text{FFL}})$, the condition is that the magnetic field vanishes at that position:

$$\mathbf{B}_{\text{tot}}(\mathbf{r}_{\text{FFL}}) = I_1 \mathbf{P}_1(\mathbf{r}_{\text{FFL}}) + I_2 \mathbf{P}_2(\mathbf{r}_{\text{FFL}}) + I_3 \mathbf{P}_3(\mathbf{r}_{\text{FFL}}) = 0$$

Since the magnetic field in the y-direction is negligible, due to our FFL topology, this yields two scalar equations:

$$I_1 P_{1x}(\mathbf{r}_{\text{FFL}}) + I_2 P_{2x}(\mathbf{r}_{\text{FFL}}) + I_3 P_{3x}(\mathbf{r}_{\text{FFL}}) = 0$$

$$I_1 P_{1z}(\mathbf{r}_{\text{FFL}}) + I_2 P_{2z}(\mathbf{r}_{\text{FFL}}) + I_3 P_{3z}(\mathbf{r}_{\text{FFL}}) = 0$$

This is an underdetermined system with two equations and three unknowns. To resolve this, we define the relative current ratios $\alpha = I_2/I_1$ and $\beta = I_3/I_1$, assuming $I_1 \neq 0$. Dividing both equations by I_1 yields:

$$P_{1x}(\mathbf{r}_{\text{FFL}}) + \alpha P_{2x}(\mathbf{r}_{\text{FFL}}) + \beta P_{3x}(\mathbf{r}_{\text{FFL}}) = 0$$

$$P_{1z}(\mathbf{r}_{\text{FFL}}) + \alpha P_{2z}(\mathbf{r}_{\text{FFL}}) + \beta P_{3z}(\mathbf{r}_{\text{FFL}}) = 0$$

This system can be solved linearly to determine α and β , which define the relative currents required in all three coils to position the FFL at any given (x,z) coordinate.

To determine the absolute current magnitudes, we introduce a third constraint: the desired FFL gradient magnitude G_{desired} . We first assume $I_1 = 1\text{A}$ and compute the total magnetic field using the previously determined ratios:

$$\mathbf{B}_{\text{tot}}(x, z) = P_1(x, z) + \alpha P_2(x, z) + \beta P_3(x, z)$$

The local gradient magnitude at $\mathbf{r}_{\text{FFL}}$ is then computed numerically, yielding G_1 , the gradient at unit current. Since the gradient scales linearly with current, the required scaling factor is $\lambda = G_{\text{desired}}/G_1$. The final currents are then:

$$I_1 = \lambda$$

$$I_2 = \lambda \alpha$$

$$I_3 = \lambda \beta$$

This approach fully determines the coil currents required to generate an FFL at a given location with a specified gradient.

Although this formulation is specific to our three-coil configuration, it generalizes to systems with more than three selection coils. In such cases, additional degrees of freedom can be used to enforce further constraints, such as minimizing total power dissipation. While prior work has demonstrated x-position FFL control with only two coils [58], such configurations lack independent control over FFL height and typically suffer from nonlinear FFL trajectories that degrade image quality. Using three or more coils ensures full control of the FFL position and gradient in the XZ plane and opens possibilities for further optimization.

5.6 Imaging Sequence

Imaging with our single-sided scanner is performed by electronically stepping the FFL across the FOV while measuring the SPIO signal at each discrete FFL position. This approach enables the acquisition of one-dimensional projections, which are subsequently reconstructed to generate tomographic images. While the general imaging procedure remains similar to that described in our previous work [58], enhancements have been made to the imaging sequence. Namely the ability to scan larger FOVs, up to 8 cm (from 4 cm), and the ability to scan the FFL at a single height (17 mm), eliminating artifacts originating from inhomogeneous spatial encoding.

Each imaging sequence begins by defining a flat FFL trajectory in the xz-plane. The trajectory consists of evenly spaced FFL positions, typically 1 mm apart, covering a user-defined FOV that is symmetric about the scanner center. For example, a 4 cm FOV ranges from -20 mm to 20 mm. The user also specifies a desired magnetic field gradient that is held constant across all FFL positions to ensure compatibility with filtered backprojection (FBP) reconstruction.

The relative coil currents needed to generate the FFL at each (x,z) location are computed using the algorithm described in Sec. 5.5. These currents are then applied to the selection coils using programmable DC power supplies (SM30-200, Delta Elektronika for

coils 1 and 2, and GENESYS+ TDK Lambda for coil 3) controlled via Ethernet. When the power supplies first form the FFL at the edge of the FOV 203 ms is waited to before measurement to allow for the system to stabilize. After the 203 ms wait time the signal is measured for 70 ms, after which the FFL is stepped to the next position. At this new FFL position there is a 47 ms wait time before data collection, this wait time is shorter since moving the FFL is less of a shock to the system than forming it. After the 47 ms wait time the signal is recorded for 70 ms. This process is repeated until the full trajectory is sampled.

To acquire 2D images, the sample is rotated in 9° increments using a stepper-motor controlled rotational stage, seen in Fig. 5.1(a). After 20 projections over 180° , the resulting sinogram is reconstructed using FBP with a Hann filter. For imaging applications requiring increased sensitivity, additional projections can be acquired by continuing rotation beyond 180° .

The ability to define a variable FOV is a major improvement in system capability. However, larger FOVs require positioning the FFL further from the scanner center, where the selection fields are weaker per unit current. This limits the maximum achievable gradient at the FOV edges, since a uniform gradient must be maintained across the scan for accurate FBP reconstruction.

Another important advancement is the ability to maintain a flat FFL trajectory at a constant height of 17 mm. In previous implementations, the FFL height varied with x-position, resulting in a curved trajectory and degradation artifacts near the edges of the FOV. Flat FFL control improves spatial uniformity, and reduces reconstruction artifacts.

Together, these improvements extend the system's imaging capability and provide more flexible control over resolution, sensitivity, and coverage.

5.7 Results

This chapter presents experimental results obtained with the enhanced single-sided FFL MPI scanner. The imaging studies in this section are used to characterize the system's performance across a range of metrics, including sensitivity, spatial resolution, field of view, and biological imaging capability. A sequence of phantom and biological experiments is used to validate the scanner under realistic imaging conditions.

5.7.1 Imaging Sensitivity Study

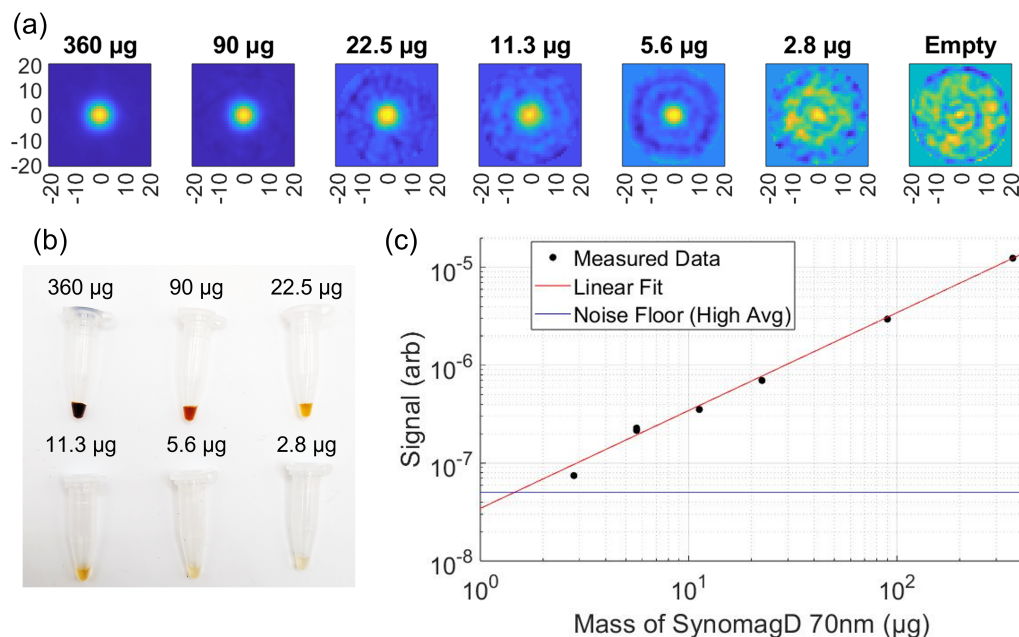


Figure 5.5: **Imaging sensitivity study.** Sensitivity characterization using a dilution series of SPIO filled microtubes. **a** Coronal slices of MPI images of six dilution phantoms containing decreasing masses of SPIO (360 to 2.8 μg). **b** Photograph of the dilution series, showing the corresponding microtubes arranged by SPIO mass. **c** Signal plotted as a function of mass of solid SPIO content on a log-log scale. Measured values show a linear relationship between signal and iron content. The red line indicates the fit, and the blue line marks the noise floor.

To evaluate the imaging sensitivity of our MPI scanner, we imaged a series of dilution phantoms filled with varying concentrations of Synomag-D 70 nm. All scans in this study were performed with a 4 cm FOV, 0.6 T/m selection gradient, and 1 mm FFL step size, corresponding to 41 FFL positions per projection. Each full projection required 5 s, and the complete sinogram was acquired over 20 angles for a total imaging time of 100 s. The excitation coil was driven at 28.9 A_{rms}, yielding an excitation field strength of 2.95 mT_{rms}.

Dilution phantoms consisted of 0.5 mL microcentrifuge tubes containing 18 µl of SPIO solution at varying dilutions: 1:1, 1:4, 1:16, 1:32, 1:64, and 1:128, as seen in Fig. 5.5(b). Based on the initial Synomag-D concentration of 20 mg/ml, these dilutions correspond to total SPIO masses of 360, 90, 22.5, 11.3, 5.6, and 2.8 µg, respectively. Assuming the SPIO solution is composed entirely of magnetite, iron comprises 72% of the total mass, yielding iron contents of 260, 65, 16.2, 8.1, 4.0, and 2.0 µg. Each phantom was positioned in the center of the imaging FOV, 17 mm above the surface of the scanner for imaging.

All samples were scanned using the standard 100 s acquisition protocol, except the three lowest concentrations (11.3, 5.6, and 2.8 µg), which were each averaged over 15 repetitions to enhance SNR, resulting in a total scan time of 25 minutes. Background noise was characterized by imaging an empty FOV under the same acquisition conditions, the maximum pixel value of this image corresponding to the noise level. MPI images and a corresponding plot of signal versus dilution are presented in Fig. 5.5(a,c). We observed a detectable signal (SNR>1) down to the 1:128 dilution, corresponding to 2.8 µg of SPIO, or 2.0 µg of iron.

5.7.2 Spatial Resolution Study

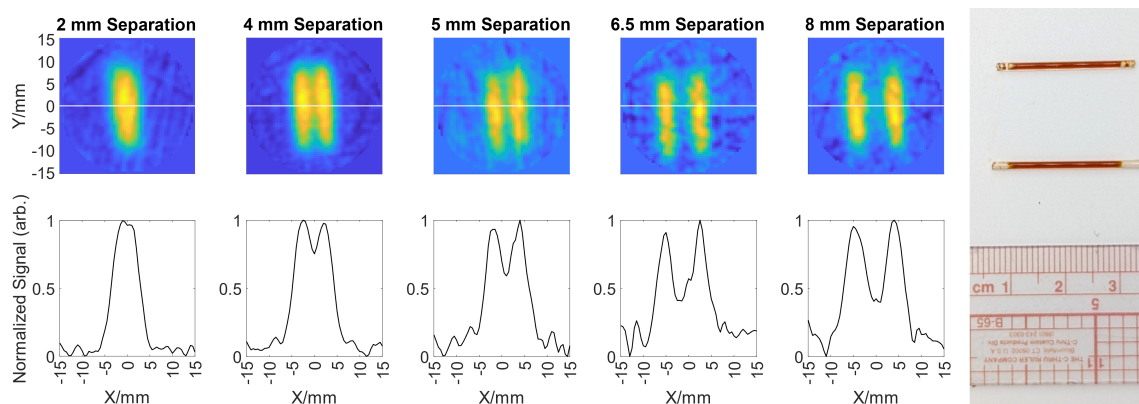


Figure 5.6: **Spatial resolution study.** Spatial resolution assessment using a two-rod phantom filled with undiluted Synomag-D 70 nm (10 mg/mL). (Top row) Reconstructed MPI images for separations of 2, 4, 5, 6.5, and 8 mm. (Bottom row) Corresponding horizontal cross-section taken across the center of each image. Rods become clearly resolvable at 4 mm separation, establishing the system's spatial resolution. (Right) Photograph of the phantom with 1 mm diameter, 20 mm long rods.

The spatial resolution of our scanner was assessed using a two-rod phantom with variable spacing. Each rod measured 20 mm in length and 1 mm in diameter and was filled with undiluted Synomag-D 70 nm SPIO at a concentration of 10 mg/mL. A photograph of the phantom is shown in Fig. 5.6.

Imaging was performed over a 3 cm FOV with a 0.5 mm FFL step size, corresponding to 61 positions per projection. The reduced FOV permitted the application of a stronger selection gradient of 1 T/m. Each projection required 7.34 s, resulting in a total acquisition time of 147 s for 20 angles. The excitation coil was driven at 20 A_{rms}, producing a excitation field strength of 2.0 mT_{rms}.

Five inter-rod spacings were tested: 2, 4, 5, 6.5, and 8 mm (side to side). As shown in Fig. 5.6 the rods were clearly distinguished at 4 mm separation, establishing a conservative spatial resolution of 4 mm.

The spatial resolution of our system may be further improved through several methods that do not require hardware modifications. Model-based iterative reconstruction algorithms have demonstrated improved resolution and noise performance in MPI [90], while post-processing techniques such as deconvolution can also enhance image sharpness. However, deconvolution is less effective in single-sided scanners due to the assumption of a spatially invariant PSF, which does not hold in systems with inherently inhomogeneous magnetic fields. In addition, MPI spatial resolution is strongly influenced by the magnetic properties of the tracer. The use of optimized SPIO formulations could therefore yield improved performance, with recent work reporting up to a tenfold resolution enhancement using advanced tracers [74].

5.7.3 Multiplanar Imaging of Rods

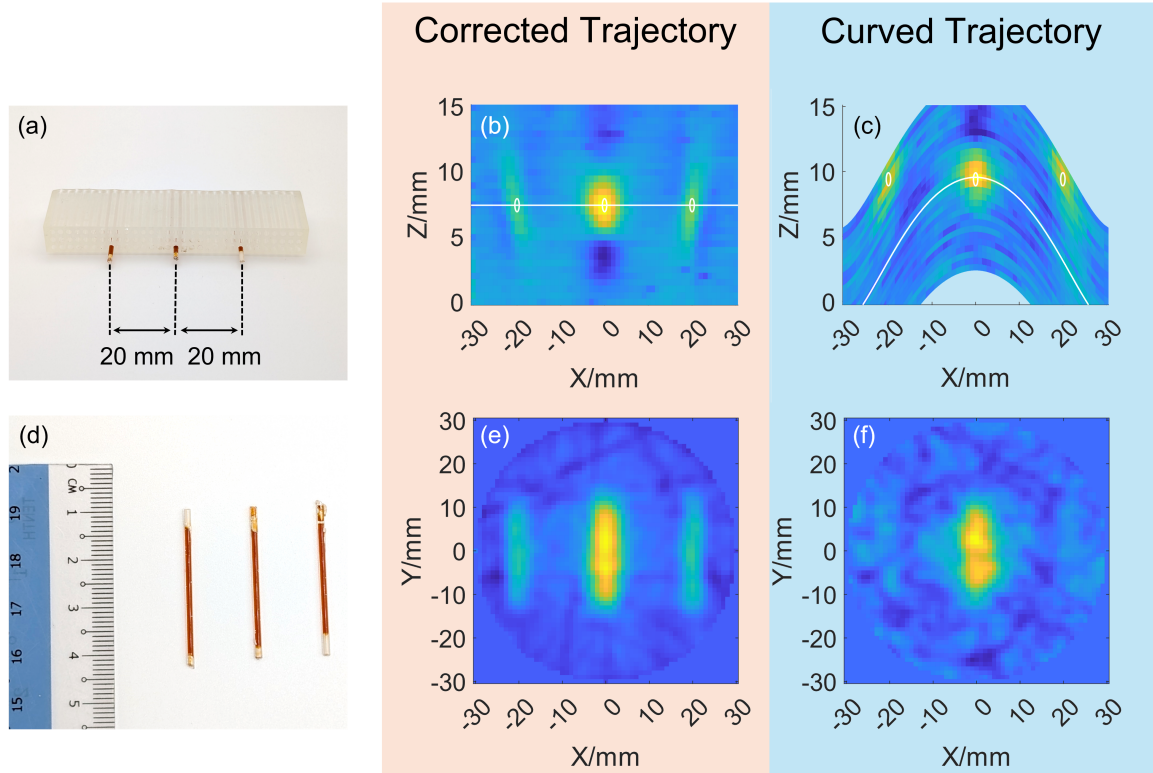


Figure 5.7: **FFL trajectory correction study** (a) Photograph of triple rod phantom in holder. (b) MPI image of triple rod phantom in the XZ plane, imaging with FFL trajectory algorithm. (c) MPI image of triple rod phantom in the XZ plane, imaging without FFL trajectory correction. (d) Photograph of SPIO rods. (e) MPI image of triple rod phantom in the XY plane. (f) MPI image of triple rod phantom in the XY plane, imaging without FFL trajectory correction.

To evaluate the effectiveness of the FFL control algorithm, we imaged a triple-rod phantom in both the XY and XZ planes. The phantom consisted of three rods (1 mm diameter, lengths 25 mm) filled with undiluted Synomag-D 70 nm SPIO at a concentration

of 10 mg/mL. The rods were aligned at the same height within a 3D printed holder and spaced 20 mm center-to-center. Photographs of the phantom and holder are shown in Fig. 5.7(a,c).

For both imaging planes, we used a 6 cm FOV with a 1 mm FFL step size, corresponding to 61 positions per projection and a 7.34 s acquisition time per projection. In the XY imaging sequence, projections were acquired at 20 different angles, resulting in a total scan time of 147 s. For the XZ image, the phantom was translated vertically in 0.5 mm increments across 31 different z-positions, corresponding to a 228 s scan time. A constant gradient of 0.6 T/m and an excitation strength of 2.0 mT_{rms} (20 A_{rms}) were used for both scans. Reconstructed MPI images of the phantom are shown in Fig. 5.7(b,d).

In the XZ image, the rods are clearly resolved at a uniform height and spaced with the expected 20 mm separation, validating the flatness of the FFL trajectory. The XY image also accurately reproduces the expected rod lengths and lateral positions. Without a flat FFL trajectory, rods would appear shorter due to deviations in the FFL height away from the center of the FOV. Thus, this study confirms that the implemented FFL control algorithm enables accurate electronic positioning of the FFL along a flat plane, essential for reliable imaging.

5.7.4 FOV Study

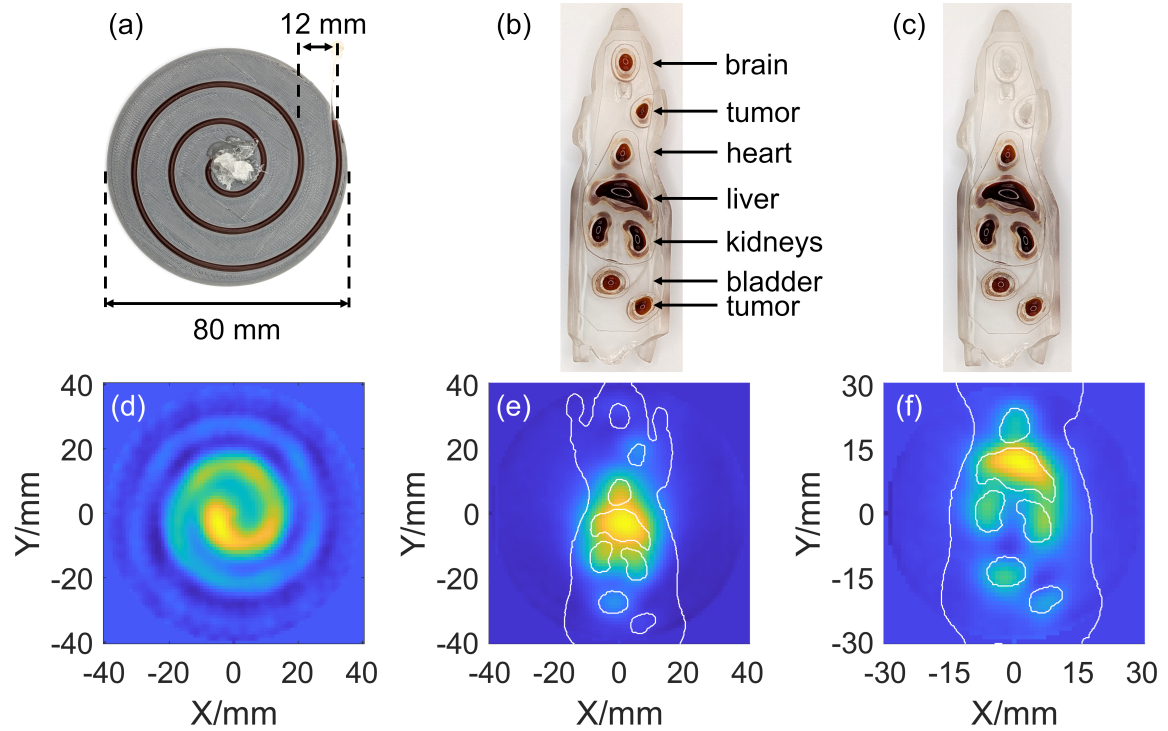


Figure 5.8: **Maximum FOV study.** (a) Photograph of the spiral phantom constructed from 1 mm inner-diameter tubing embedded in a 3D-printed former. (b–c) Photographs of the anatomic mouse phantom with labeled organ and tumor compartments filled with Vivotrax SPIO. (d) Reconstructed MPI image of the spiral phantom. (e) Reconstructed MPI image of the mouse phantom acquired with an 8 cm FOV (gradient 0.4 T/m). (f) Reconstructed MPI image of the same phantom acquired with a 6 cm FOV (gradient 0.6 T/m).

To demonstrate the extended imaging FOV enabled by these upgrades, we imaged two phantoms entirely in the FOV: a planar spiral phantom and an anatomically shaped mouse phantom in the coronal plane. The mouse phantom includes compartments representing major organs and two “tumor” volumes, each filled with a 1:2 dilution of

Vivotrax (Magnetic Insight, USA) SPIO. The spiral phantom was constructed from 1 mm inner diameter tubing embedded in a flat 3D-printed former, filled with undiluted (10 mg/mL) Synomag-D 70 nm SPIO, forming three full turns with an initial radius of 35 mm and a radial taper of 12 mm per turn. Photographs of both phantoms are shown in Fig. 5.8.

Both phantoms were imaged using an 8 cm FOV with a 1 mm FFL step size, resulting in 81 discrete FFL positions per projection. A gradient strength of 0.4 T/m and an excitation field of 1.8 mT ($I_{\text{RMS}} = 18$ A) were used for all scans. Each projection required 9.68 s, corresponding to a total imaging time of 194 s (20 angles). Reconstructed MPI images of both phantoms are shown in Fig. 5.8.

Signal fading is observed near the edges of the 8 cm FOV for both phantoms, as shown in Fig. 5.8(d,e), due to the receive coil's sensitivity profile, which is weaker further from the center of the FOV. To recover imaging homogeneity and improve spatial resolution, the mouse phantom was also imaged using a reduced 6 cm FOV, which allowed the gradient to be increased to 0.6 T/m. In this experiment, all organ compartments were filled except the brain and upper tumor volumes. The scan was performed with a 0.5 mm FFL step size, yielding 61 discrete FFL positions per projection. The excitation field was maintained at 1.8 mT ($I_{\text{RMS}} = 18$ A), and each projection required 7.34 s, resulting in a total imaging time of 147 s (20 angles). The reconstructed image for this configuration is shown in Fig. 5.8(d).

5.7.5 Preliminary In-Vitro Imaging Experiments

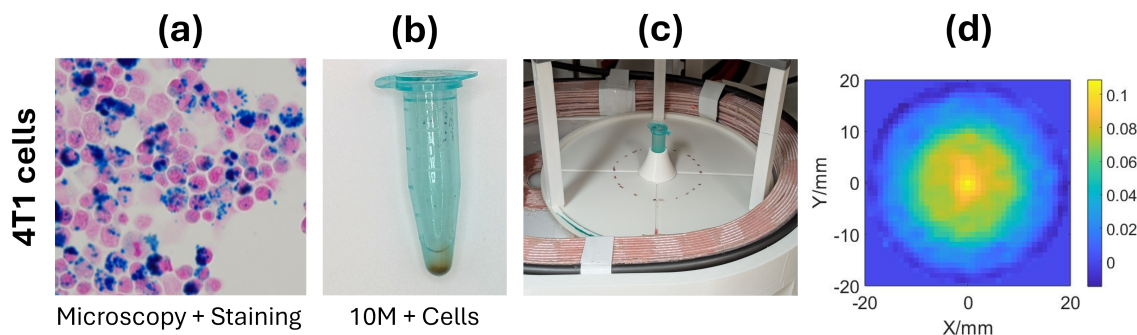


Figure 5.9: **In-vitro imaging study.** Imaging results of SPIO labeled cancer cells using the single-sided MPI scanner. (a) Microscopy image of stained 4T1 cells confirming tracer uptake. (b) Photograph of labeled cells suspended in PBS within 1.5 mL microcentrifuge tubes ($>10M$ 4T1 cells). (c) Photograph of the tube positioned at the center of the scanner's sample table for imaging. (d) Resulting MPI image of tracer labeled cells.

A preliminary in-vitro imaging experiment was conducted to assess the scanner's capability to detect SPIO labeled biological samples. Our collaborators at Henry Ford Hospital prepared a cancer cell strain¹, derived from a murine breast cancer line (4T1). The cell population was incubated with Vivotrax Plus tracer particles to enable SPIO uptake by the cells, after which unbound particles were washed away. The labeled cells were resuspended in PBS with a total suspension volume of 250 μL and transferred into 1.5 mL microcentrifuge tubes, as shown in Fig. 5.9 (b). Successful SPIO binding was confirmed using optical microscopy of stained samples, shown in Fig. 5.9 (a).

¹Cell samples were prepared according to approved institutional biosafety protocols (see Appendix C for IBC Protocol Approval).

The micro centrifuge tube was positioned at the center of the scanner's FOV for imaging, as shown in Fig. 5.9 (c). Imaging was performed using a total acquisition time of 25 minutes over an 8 cm FOV, with a discrete step size of 2 mm per projection. A magnetic field gradient of 0.4 T/m was applied, and excitation strength was 3.1 mT_{rms}. The resulting MPI images, shown in Fig. 5.9 (d), clearly demonstrate localized signal from the labeled cell sample, confirming that the scanner's sensitivity is sufficient for in-vitro cell detection.

This experiment represents the first demonstration of in-vitro imaging using a single-sided MPI system and marks an important step toward its biomedical translation. Detecting SPIO bound within cells represents a particularly challenging case for MPI, as intracellular SPIO typically produces weaker signals than freely dispersed particles. In vivo, most tracer accumulation in tumors occurs extracellularly through the enhanced permeability and retention (EPR) effect rather than direct cellular uptake. Therefore, successful detection of SPIO confined within cells indicates that the scanner has achieved tumor relevant sensitivity, as intracellularly bound SPIO represents a conservative, or “worst-case” scenario of the tumor microenvironment.

5.7.6 Preliminary In-Vivo Imaging

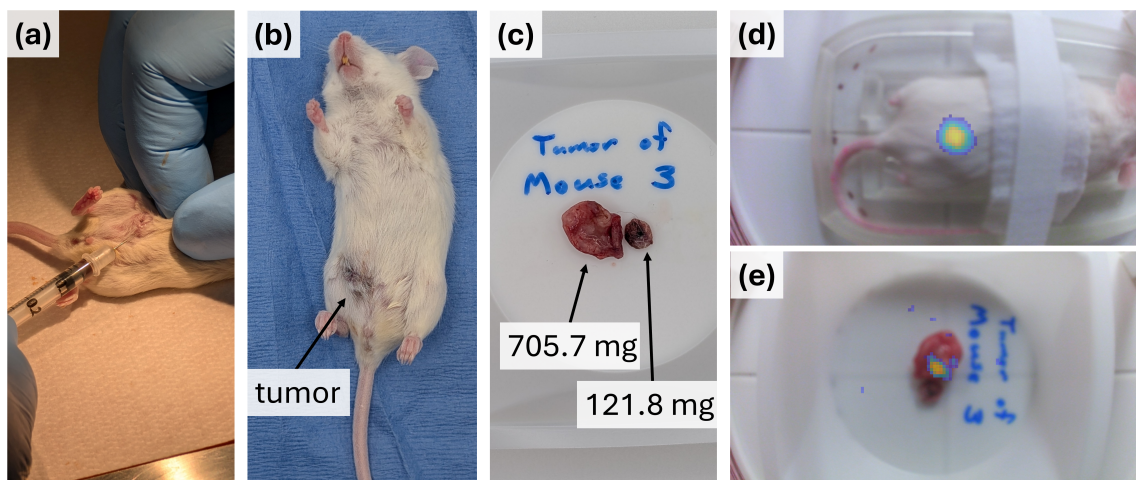


Figure 5.10: **Preliminary in-vivo imaging of a mouse tumor.** (a) Intratumoral injection of SPIO tracer into a subcutaneous tumor. (b) Photograph of the mouse prior to imaging with the tumor location visible. (c) Excised tumor shown with measured masses. (d) MPI image of the mouse coregistered with a photograph inside the scanner. (e) MPI image of the excised tumor coregistered with a photograph acquired during ex-vivo imaging.

In addition to the in-vitro cell imaging experiments, in-vivo imaging was performed to demonstrate the biological relevance of the single-sided MPI scanner. This section presents preliminary in-vivo imaging of a tumor in a mouse, extending the imaging experiments from isolated biological samples to a living subject.

A mouse bearing a subcutaneous 4T1 tumor xenograft was prepared for imaging by collaborators at Henry Ford Hospital. Prior to imaging, the mouse was injected intratumorally with 30 μ L of Synomag-D (70 nm, plain) to localize tracer within the tumor volume, as shown in Fig. 5.10(a). A photograph of the mouse prior to imaging, with the tumor location visible, is shown in Fig. 5.10(b). All animal handling and tracer

administration were performed by trained and approved personnel under an IACUC protocol (approval shown in Appendix C), and the author's role was limited to image acquisition.

During imaging, the mouse was positioned prone within the scanner, as shown in Fig. 5.10(d). Imaging was performed using an 8 cm FOV with a discrete FFL step size of 1 mm, resulting in 81 FFL positions per projection. A magnetic field gradient strength of 0.4 T/m was applied, and the excitation field amplitude was 2.7 mT_{rms} (27.7 A_{rms}). Each projection required 9.68 s, and a total of 20 projection angles were acquired, yielding a total imaging time of 194 s.

The resulting MPI image is shown in Fig. 5.10(d), coregistered with a photograph of the mouse positioned inside the scanner. The reconstructed image shows a localized signal originating from the tumor region, with no significant signal observed elsewhere. At the end of the imaging session, the tumor was excised later the same day, approximately six hours after the in-vivo scan. The excised tumor was weighed and subsequently imaged ex vivo. The excised tumor and corresponding MPI images are shown in Fig. 5.10(c,e), confirming that the detected signal originates from the tumor.

These preliminary results demonstrate that the single-sided MPI scanner is capable of tumor detection and delineation. Together with the in-vitro cell imaging experiments presented in the previous section, this result demonstrates the potential of this scanner geometry, and marks an important step towards clinical translation.

5.8 Conclusion

This chapter presented the next generation of the FFL MPI scanner featuring a hybrid surface-volume excitation coil, providing a semi-homogeneous magnetic field over an 8 cm FOV, addressing a challenge inherent to single-sided systems. In addition to hardware upgrades, a new algorithm was implemented for electronic FFL trajectory control, enabling flat scans across extended FOVs. These hardware and software

enhancements improve the scanner's performance and clinical viability by mitigating field inhomogeneity and enabling linear spatial encoding.

The sensitivity study demonstrated reliable detection of a 1:128 dilution, corresponding to 2.8 μg (2.0 μg of iron). Extrapolating the linear fit to the data (see Fig. 5.5) to the background level (SNR=1) implies that we should be able to reach a sensitivity of 1.0 μg of iron content, providing a lowered noise level. This meets a clinically relevant sensitivity threshold of 4.8 μg for tumor imaging, based on a 400 mg iron dose, 1% ID/g tumor uptake, and 1.2 mg tumor mass, bringing us closer to our desired application of breast tumor detection. In this study, the excitation field was limited to 2.95 mT due to heating of the excitation coil, resulting in current instabilities. Higher excitation fields, and therefore improved sensitivity, could be achieved through more efficient cooling of the excitation coil. This could be implemented by submerging the coil in a thermal bath or constructing it from hollow conductors with internal water flow.

The spatial resolution study demonstrated a 4 mm resolution, defined by the minimum distinguishable separation between two SPIO-filled rods. This resolution was achieved using FBP without additional enhancements from iterative reconstruction or deconvolution. The demonstrated 4 mm resolution is clinically relevant for breast cancer applications, which are a primary focus of this system. The median tumor size detected by current screening modalities is 7.5 mm [91], and most early-stage tumors fall within the 5-10 mm range. Moreover, MPI's zero signal from tissue allows for the detection of lesions smaller than the nominal resolution, provided adequate sensitivity. Clinically, breast-conserving surgery typically recommends a minimum margin of 2 mm [92], suggesting that a spatial resolution of 4 mm is sufficient to support margin assessment. These results demonstrate the scanner's suitable spatial resolution for breast imaging and its potential utility for surgical planning and guidance.

The accuracy and utility of the FFL trajectory control algorithm were demonstrated in the flat trajectory study, where a triple-rod phantom was imaged in both the XY and XZ planes with and without correction. Without trajectory correction, the reconstructed images exhibited significant artifacts, including distorted geometry and missing rods. These artifacts result from the nonlinear FFL trajectory, which causes inconsistent spatial encoding across the FOV. In contrast, with the correction algorithm applied, all rods were clearly visualized in both imaging planes with accurate lengths, spacing, and positions. These results confirm that the trajectory correction algorithm performs as intended and extends the usable imaging FOV beyond the previous 4 cm limit.

The extended 8 cm FOV was validated using two phantoms: a spiral phantom and a mouse phantom with anatomical volumes. Both were successfully imaged over the full FOV, demonstrating the system's ability to accommodate extended geometries and larger subjects. An 8 cm FOV represents a substantial advance for single-sided MPI scanners and is larger than that of leading commercial preclinical systems. For example, the Magnetic Insight Momentum offers a 6 cm lateral FOV, while the Bruker MPI scanner provides a 5 cm lateral FOV.

While the 8 cm FOV was successfully imaged, signal attenuation was observed at the FOV edges (Fig. 5.8). This attenuation is attributed to the sensitivity profile of the 7 cm diameter receive coil, which loses sensitivity towards the edges of the 8 cm FOV. Increasing the size of the receive coil would enhance sensitivity homogeneity across the 8 cm FOV. However, with our current receive gradiometer design [79], scaling the receive coil necessitates scaling the gradiometer, as cancellation relies on an identical receive gradiometer pair. Due to geometric constraints imposed by the surface-volume excitation coil (Fig. 5.2), the receive gradiometer pair cannot be scaled beyond 7 cm. Consequently, for a symmetric receive gradiometer system, 8 cm represents the maximum FOV.

Homogeneity can be recovered by reducing the FOV, as shown in the mouse phantom study. Restricting the FOV to 6 cm confines the imaging region to the semi-homogeneous zone of the receive coil's sensitivity profile, resulting in a more uniform image. This "zoomed" FOV also permits operation at a higher gradient strength of 0.6 T/m, which restores resolvability between organs such as the kidneys (Fig. 5.8d). Comparing the full-FOV image (Fig. 5.8e) to the zoomed image (Fig. 5.8f) demonstrates that both image uniformity and organ resolvability are possible when the FOV is zoomed to this region.

Future work will aim to extend homogeneity across the entire 8 cm FOV through both hardware and software improvements. On the hardware side, alternative receive–gradiometer designs could be explored to achieve a more homogeneous sensitivity profile across larger FOVs. On the software side, scanner performance could be further enhanced through an image reconstruction upgrade. In this work, reconstruction was accomplished with FBP, without post-processing. Replacing FBP with model-based iterative reconstruction that incorporates a measured or simulated system function should raise both sensitivity and spatial resolution [90], additionally, this could correct for the current limited sensitivity profile of the receive coil, eliminating the inhomogeneity at the edges of the large FOV (8 cm). Alternatively, post-processing techniques, such as deconvolution or machine-learning techniques, could further enhance scanner performance as well. Standard deconvolution techniques are challenging in single-sided systems because they assume spatially invariant point-spread functions, which is a challenging assumption for scanners with inhomogeneous magnetic fields. Although single-sided scanners to this date feature inhomogeneity in imaging, this may be mitigated in the future.

CHAPTER SIX

CONCLUSION

6.1 Summary and Conclusion

This dissertation presents the design, development, characterization, and experimental validation of a single-sided FFL MPI scanner with the ultimate goal of enabling anatomically targeted, human-scale imaging, with a focus on breast imaging applications. Breast imaging represents a clinically significant application, as breast cancer remains one of the most prevalent cancers worldwide and early, sensitive detection promises improved patient outcomes. The central motivation of this work was to advance MPI hardware toward clinical relevance by addressing challenges that currently restrict MPI from human imaging applications, including scalability, sensitivity, and anatomic accessibility.

Chapter 1 established the clinical and technical motivation for this work by reviewing the current landscape of breast imaging and the state of MPI technology. The chapter introduced MPI as a tracer-based imaging modality with high sensitivity, positive contrast, and no ionizing radiation, making it attractive for many applications including tumor detection. The limitations of conventional closed-bore MPI scanners were discussed, particularly their inability to scale to full-body human FOVs due to power constraints. Single-sided scanner geometries were presented as a promising alternative for anatomically targeted imaging, especially for anatomies such as the breast, where open access is essential. The chapter concluded by positioning the single-sided FFL scanner developed in this dissertation as a novel and competitive approach within the broader context of human-scale MPI development.

	Prototype Single-Sided FFL Scanner ¹	Enhanced Single-Sided FFL Scanner ²	Other Human Scanners ³
Drive Amplitude (mT)	0.9	4.0	6–7
Gradient (T/m)	0.58	1.0	0.2–1.0
Sensitivity ($\mu\text{g Fe}$)	6.0*	2.0	1.0–19
Spatial Resolution (horizontal, mm)	6.5**	< 4.0	—
Maximum FOV (cm^2)	4.0×4.0	8.0×8.0	—

* Theoretically estimated sensitivity.

** Obtained with PSF deconvolution.

¹ [58]

² [88]

³ [32], [35], [36], [38]

Table 6.1: Comparison of metrics of MPI scanners.

Chapter 2 developed the theoretical foundation underlying the unique imaging methodology of our scanner. MPI was framed as a small signal detection problem, emphasizing the challenge of detecting small tracer induced signals in the presence of a large ($\times 10^6$) background signal. The generation and control of the FFL was analyzed, along with the discrete stepping acquisition strategy used to achieve robust spatial encoding in the presence of inhomogeneous magnetic fields inherent to a single-sided geometry. Specific to our unique scanner configuration and imaging method the signal equation was derived and examined under simplifying limits to illuminate its dependence on tracer properties, and excitation field. Narrowband imaging using third harmonic detection was then introduced as a practical and robust strategy for background suppression, and its implications for spatial resolution and PSF behavior were analyzed in detail.

Chapter 3 presented a custom made simulation toolset designed to model the single-sided MPI scanner and enable rapid prototyping prior to experimental implementation. Biot–Savart based electromagnetic simulations were used to characterize the magnetic fields generated by all scanner coils, including the selection coils, receive coil, and excitation coil. These simulations allowed for prototyping of the receive coil and the surface–volume excitation coil prior to construction. In addition to electromagnetic modeling, imaging simulations were developed to model signal generation, signal detection, and image reconstruction. These simulations enabled testing and validation of imaging methodology before implementation on the physical scanner. In addition, they also allowed for generation of synthetic datasets, which were used to explore machine learning approaches for image enhancement. Neural network architectures, including an autoencoder and a U-Net, were evaluated using simulated data, demonstrating their ability to suppress artifacts and improve spatial fidelity in reconstructed images.

Chapter 4 described the construction and experimental validation of the initial prototype single-sided FFL MPI scanner. The hardware architecture, signal acquisition chain, spatial encoding strategy, and imaging sequence were detailed. Using this prototype system, a series of phantom imaging studies were performed to demonstrate imaging capabilities, including dual plane imaging of rod phantoms, 3D imaging of simple geometries, and tomographic imaging of anatomical phantoms. Notably, imaging of artificial tumors embedded in an anatomical breast phantom demonstrated the feasibility of using a single-sided FFL MPI scanner for breast sized volumes and complex geometries. This capability is unique to the single-sided geometry presented in this work, as no existing MPI scanner is able to accommodate and image a full, anatomically realistic breast shaped phantom.

Despite the initial success of the original prototype single-sided scanner, this implementation suffered from challenges historically associated with single-sided

geometries. Most notably, subpar overall sensitivity, which limited imaging to phantom studies rather than biological subjects. In addition, the original system employed only two selection coils, resulting in non-linear spatial encoding that restricted the usable FOV and introduced reconstruction artifacts. To address these limitations, a series of targeted hardware and software upgrades were designed and implemented, as described in Chapter 5. Central to these improvements was the development of a surface–volume excitation coil, a novel concept for the field of MPI, which significantly enhanced excitation strength and field homogeneity at depth. The introduction of this new excitation geometry also freed the original excitation coil to be repurposed as an auxiliary selection coil, enabling the implementation of a new linear spatial encoding algorithm.

Following implementation of these upgrades imaging studies were performed to characterize the enhanced scanner’s technical performance. Phantom imaging experiments demonstrated substantial improvements in sensitivity, spatial resolution, FOV, and image fidelity compared to the original prototype, elevating the system to performance levels comparable to and in some cases exceeding those of other reported human-scale MPI prototype scanners (Table 6.1). Importantly, the increased sensitivity enabled imaging of biological samples, including in vitro imaging of labeled cancer cells and preliminary in vivo imaging in a mouse tumor model. The successful in vivo mouse imaging study represents a significant breakthrough for single-sided MPI as a whole, as prior demonstrations of this topology had been limited to simple phantom imaging. These results further demonstrate the feasibility of the proposed scanner design for tumor detection tasks.

Taken together, the work presented in this dissertation demonstrates that single-sided FFL MPI is a viable and competitive approach for human scale imaging, specifically targeting breast applications. Through a combination of theoretical analysis, simulation driven design, and iterative experimental validation, the scanner developed in

this work overcomes several limitations that have historically constrained single-sided MPI, including insufficient sensitivity, and non-linear spatial encoding. The enhanced system achieves performance metrics comparable to other human scale MPI prototypes, at significantly lower development cost, while uniquely enabling imaging of anatomically realistic breast sized volumes. Importantly, the progression from phantom imaging to biologically relevant in vitro and in vivo studies establishes a pathway toward translational applications. While further development is required before clinical deployment, the results of this dissertation position single-sided FFL MPI as a promising platform for future breast imaging and tumor detection studies, and more broadly contribute to ongoing efforts to extend MPI beyond the preclinical setting and toward human imaging applications.

6.2 Academic Contributions

6.2.1 Publications

Papers:

1. **Christopher McDonough**, John Chrisekos, Matthew Jurj, Alycen Wiacek, and Alexey Tonyushkin. "Imaging of artificial tumor models in an anatomical breast phantom with a single-sided magnetic particle imaging scanner." Tomography (Under Review).
2. **Christopher McDonough**, John Chrisekos, Cody Hunt, and Alexey Tonyushkin. "Enhanced performance of a single-sided MPI scanner with a hybrid surface-volume excitation coil." Physics in Medicine & Biology 70, no. 23 (2025): 235015. [88]
3. **Christopher McDonough**, John Chrisekos, and Alexey Tonyushkin. "Tomographic Magnetic Particle Imaging with a Single-Sided Field-Free Line Scanner." IEEE Transactions on Biomedical Engineering 71, no. 12 (2024): 3470-3481. [58]

4. **Christopher McDonough**, Jason Pagan, and Alexey Tonyushkin. "Implementation of the surface gradiometer receive coils for the improved detection limit and sensitivity in the single-sided MPI scanner." *Physics in Medicine & Biology* 67, no. 24 (2022): 245009. [79]
5. **Christopher McDonough**, David Newey, and Alexey Tonyushkin. "1-d imaging of a superparamagnetic iron oxide nanoparticle distribution by a single-sided ffl magnetic particle imaging scanner." *IEEE transactions on magnetics* 58, no. 8 (2022): 1-5. [62]
6. Carlos Chinchilla, **Christopher McDonough**, Amanuel Negash, Jason Pagan, and Alexey Tonyushkin. "2D projection image reconstruction for field free line single-sided magnetic particle imaging scanner: simulation studies." *International journal on magnetic particle imaging* 7, no. 1 (2021): 2104001. [86]
7. Jason Pagan, **Christopher McDonough**, Triet Vo, and Alexey Tonyushkin. "Single-sided magnetic particle imaging device with field-free-line geometry for in vivo imaging applications." *IEEE Transactions on Magnetism* 57, no. 2 (2020): 1-5. [82]

Proceedings:

1. **Christopher McDonough**, John Chrisekos, and Alexey Tonyushkin. "Design and Implementation of a Novel Surface Excitation Coil for a Single-Sided Field Free Line MPI Scanner." *International Journal on Magnetic Particle Imaging IJMPI* 11, no. 1 Suppl 1 (2025). [93]
2. Alexey Tonyushkin, and **Christopher McDonough**. "Tomographic Imaging of Implanted Tumors in a Breast Phantom with a Single-Sided MPI Scanner."

International Journal on Magnetic Particle Imaging IJMPI 11, no. 1 Suppl 1 (2025). [94]

3. **Christopher McDonough**, John Chrisekos, and Alexey Tonyushkin. "Multiplanar Imaging with a Single-Sided MPI Scanner." In 2024 IEEE International Magnetic Conference-Short papers (INTERMAG Short papers), pp. 1-2. IEEE, 2024. [95]
4. **Christopher McDonough**, John Chrisekos, and Alexey Tonyushkin. "Dual mode imaging of phantoms in two orthogonal planes with a single-sided FFL MPI scanner." International Journal on Magnetic Particle Imaging IJMPI 10, no. 1 Suppl 1 (2024). [96]
5. **Christopher McDonough**, and Alexey Tonyushkin. "2d projection imaging with a single-sided ffl magnetic particle imaging scanner." International Journal on Magnetic Particle Imaging IJMPI 9, no. 1 Suppl 1 (2023). [97]
6. **Christopher McDonough**, and Alexey Tonyushkin. "Demonstration of the new detection limit for the single-sided FFL MPI scanner with a surface gradiometer receive coils." International Journal on Magnetic Particle Imaging IJMPI 8, no. 1 Suppl 1 (2022). [98]
7. **Christopher McDonough**, and Alexey Tonyushkin. "1D Imaging with a Single-Sided FFL Magnetic Particle Imaging Scanner." International Journal on Magnetic Particle Imaging IJMPI 8, no. 1 Suppl 1 (2022). [98]
8. Carlos Chinchilla, **Chris McDonough**, Amanuel Negash, Jason Pagan, and Alexey A. Tonyushkin. "Simulation Studies of Image Reconstruction for Field Free Line Single-Sided Magnetic Particle Imaging." International Journal on Magnetic Particle Imaging IJMPI 6, no. 2 Suppl 1 (2020). [99]

Patents:

1. 63/958,739. Alexey Tonyushkin, **Christopher McDonough**, “System and Method for Detecting DC Magnetic Fields”. 2026 (Provisional)
2. PCT/US26/17249. Alexey Tonyushkin, **Christopher McDonough**, “System and Method for Organ Specific Surface Excitation Coil for a Single-Sided Magnetic Particle Imaging”. 2026 (Applied)

6.2.2 Presentations

Talks:

1. **Christopher McDonough**, and Alexey Tonyushkin, "Design, characterization and validation of a single-sided field free line scanner for magnetic particle imaging", APS March Meeting 2026, Denver CO, USA, Invited, Outstanding Doctoral Dissertation in Medical Physics
2. **Christopher McDonough**, John Chrisekos, and Alexey Tonyushkin, "Enhanced Capabilities of Single-Sided MPI Scanner Towards Clinical Applications", World Molecular Imaging Conference 2025, Anchorage AK, USA
3. **Christopher McDonough**, Matthew Jurj, and Alexey Tonyushkin, "Enhanced Imaging Capabilities of a Single-Sided Magnetic Particle Imaging Scanner for Large Phantoms", Joint Conference on Magnetism and Magnetic Materials and Intermag 2025, New Orleans LA, USA
4. **Christopher McDonough**, Chris Bastajian, Alycen Wiacek, and Alexey Tonyushkin, "Image Reconstruction for a Shift Variant Magnetic Particle Imaging system using Deep Learning", APS March Meeting 2024, Minneapolis MN, USA

5. **Christopher McDonough**, and Alexey Tonyushkin, "Magnetic Particle Imaging with a Single-Sided Scanner", APS EGLS Spring Meeting 2023, Auburn Hills MI, USA
6. **Christopher McDonough**, and Alexey Tonyushkin, "Two-dimensional imaging using a single-sided magnetic particle imaging scanner", APS March Meeting 2023, Las Vegas NV, USA
7. **Christopher McDonough**, and Alexey Tonyushkin, "Two-dimensional imaging using a single-sided magnetic particle imaging scanner", Magnetism and Magnetic Materials Meeting 2022, Minneapolis MN, USA

Posters:

1. **Christopher McDonough**, John Chrisekos, Tanjim Siddiqua, and Alexey Tonyushkin, "Enhanced Capabilities of Single-Sided MPI Scanner Towards Clinical Applications", World Molecular Imaging Conference 2025, Anchorage AK, USA
2. **Christopher McDonough**, John Chrisekos, and Alexey Tonyushkin, "Design and Implementation of a Novel Surface Excitation Coil for a Single-Sided Field Free Line MPI Scanner", International Workshop on Magnetic Particle Imaging 2025, Lübeck, Germany
3. **Christopher McDonough**, Matthew Jurj, and Alexey Tonyushkin, "Tomographic Imaging of Implanted Tumors in the Anatomical Breast Phantom with a Single-Sided Magnetic Particle Imaging Scanner", World Molecular Imaging Conference 2024, Montréal Quebec, Canada
4. **Christopher McDonough**, John Chrisekos, and Alexey Tonyushkin, "Multidimensional Imaging of Phantoms with a Single-Sided Magnetic Particle

Imaging Scanner", Magnetism and Magnetic Materials Meeting 2023, Dallas TX, USA

5. **Christopher McDonough**, and Alexey Tonyushkin, "Two-dimensional imaging using a single-sided field-free line magnetic particle imaging scanner", MagMeet 2023, Greenville SC, USA
6. **Christopher McDonough**, and Alexey Tonyushkin, 1D "Imaging with a Single-Sided FFL Magnetic Particle Imaging Scanner", International Workshop on Magnetic Particle Imaging 2022, Virtual Attendance

6.2.3 Abstracts

Abstracts:

1. Chris Bastajian, **Christopher McDonough**, Cody Hunt, Matthew Jurj, and Alexey Tonyushkin. "Study of Oversized SPIO Nanoparticles with a Magnetic Particle Spectrometer for Suitability as MPI Tracers." Bulletin of the American Physical Society (2025). [100]
2. Chris Bastajian, **Christopher McDonough**, John Chrissekos, and Alexey Tonyushkin. "Magnetic Particle Spectrometer for Characterization of Superparamagnetic Iron Oxide Nanoparticles." Bulletin of the American Physical Society (2024). [101]
3. **Christopher McDonough**, Christopher Bastajian, Alycen Wiacek, and Alexey Tonyushkin. "Image reconstruction for a shift variant magnetic particle imaging system using deep learning." Bulletin of the American Physical Society (2024). [102]

4. **Christopher McDonough**, and Alexey Tonyushkin. "Two Dimensional Imaging Using a Single-Sided Field Free Line Magnetic Particle Scanner." Bulletin of the American Physical Society (2023). [103]
5. Alexey Tonyushkin, **Christopher McDonough**, and David Newey. "Magnetic Particle Imaging Using a Single Sided Field Free Line Scanner." Bulletin of the American Physical Society (2022). [104]

APPENDIX A
THEORY AND CALCULATIONS

A.1 Langevin Derivation of Paramagnetism

The Langevin equation describes the equilibrium magnetization M of a system of non-interacting paramagnetic particles subjected to an external magnetic field H . Each particle possesses a magnetic moment μ , and the ensemble is assumed to be in thermal equilibrium at temperature T .

A.1.1 Statistical Mechanics of Magnetic Moments

In an external magnetic field, the potential energy U of a magnetic moment μ oriented at an angle θ with respect to the field direction is given by:

$$U(\theta) = -\mu H \cos \theta \quad (\text{A.1})$$

The probability density of a magnetic moment adopting a particular orientation is governed by the Boltzmann distribution:

$$P(\theta) = \frac{\exp\left(\frac{\mu H \cos \theta}{k_B T}\right)}{Z} \quad (\text{A.2})$$

where k_B is the Boltzmann constant, T is the temperature, and Z is the partition function ensuring normalization:

$$Z = \int_0^\pi \exp\left(\frac{\mu H \cos \theta}{k_B T}\right) \sin \theta d\theta \quad (\text{A.3})$$

Make the substitution $u = \frac{\mu H \cos \theta}{k_B T}$, so that $du = -\frac{\mu H \cos \theta}{\sin} \theta d\theta$ gives the following integral:

$$Z = \frac{k_B T}{\mu H} \int_{\frac{\mu H}{k_B T}}^{\frac{\mu H}{-k_B T}} \exp(u) du = \frac{k_B T}{\mu H} \exp(u) \Big|_{\frac{\mu H}{-k_B T}}^{\frac{\mu H}{k_B T}} = \frac{2k_B T}{\mu H} \sinh\left(\frac{\mu H}{k_B T}\right) \quad (\text{A.4})$$

A.1.2 Ensemble Averaged Magnetization

The component of the magnetic moment along the field direction is $\mu \cos \theta$. The ensemble average of this component yields the magnetization per particle:

$$\langle \mu_z \rangle = \langle \mu \cos \theta \rangle = \mu \int_0^\pi \cos \theta P(\theta) \sin \theta d\theta \quad (\text{A.5})$$

Substituting the expression for $P(\theta)$ and simplifying, we obtain:

$$\langle \mu_z \rangle = \frac{\mu}{Z} \int_0^\pi \cos \theta \exp \left(\frac{\mu H \cos \theta}{k_B T} \right) \sin \theta d\theta \quad (\text{A.6})$$

Make the substitution $x = \cos \theta$, so that $dx = -\sin \theta d\theta$, and the limits of integration change from $\theta = 0$ to π into $x = 1$ to -1 . This gives:

$$\langle \mu_z \rangle = \frac{\mu}{Z} \int_{-1}^1 x \exp \left(\frac{\mu H x}{k_B T} \right) dx = \mu \left[\coth \left(\frac{\mu H}{k_B T} \right) - \frac{k_B T}{\mu H} \right] \quad (\text{A.7})$$

A.1.3 Langevin Function

Define the dimensionless parameter:

$$\xi = \frac{\mu H}{k_B T} \quad (\text{A.8})$$

Then the average magnetic moment along the field direction becomes:

$$\langle \mu_z \rangle = \mu \left[\coth(\xi) - \frac{1}{\xi} \right] = \mu \mathcal{L}(\xi) \quad (\text{A.9})$$

where

$$\mathcal{L}(\xi) = \coth(\xi) - \frac{1}{\xi} \quad (\text{A.10})$$

is the *Langevin function*.

A.1.4 Total Magnetization

For a system containing N non-interacting magnetic particles per unit volume, the total magnetization is:

$$M = N\langle\mu_z\rangle = N\mu\mathcal{L}(\xi) = N\mu\left[\coth\left(\frac{\mu H}{k_B T}\right) - \frac{k_B T}{\mu H}\right] \quad (\text{A.11})$$

A.2 Curie's Law Derivation

Langevin theory describes the magnetization of a superparamagnetic nanoparticle ensemble in thermal equilibrium. The magnetization response to an applied magnetic field $\vec{H}$ is given by

$$\vec{M}(\vec{H}) = cm\mathcal{L}(\beta|\vec{H}|)\hat{H}, \quad (\text{A.12})$$

where c is the particle concentration, m is the magnetic moment of a single particle, and $\mathcal{L}(x)$ is the Langevin function defined as

$$\mathcal{L}(x) = \coth(x) - \frac{1}{x}. \quad (\text{A.13})$$

The parameter β represents the ratio of magnetic to thermal energy and is given by

$$\beta = \frac{\mu_0 m}{k_B T}, \quad (\text{A.14})$$

where μ_0 is the vacuum permeability, k_B is Boltzmann's constant, and T is the absolute temperature.

In the limit of weak applied fields, where $\beta|\vec{H}| \ll 1$, the Langevin function can be approximated by its first-order Taylor expansion,

$$\mathcal{L}(\beta|\vec{H}|) \approx \frac{\beta|\vec{H}|}{3}. \quad (\text{A.15})$$

Substituting this approximation into the Langevin magnetization expression yields

$$\vec{M}(\vec{H}) \approx \frac{cm^2\mu_0}{3k_B T} \vec{H}. \quad (\text{A.16})$$

This linear relationship between magnetization and applied magnetic field is the classical expression for paramagnetism, commonly known as Curie's law. This result demonstrates that paramagnetism is simply the low-field limit of superparamagnetism, differing primarily in the scale of the particle's magnetic moment.

A.3 Proof of the Law of Reciprocity

This appendix section provides a proof of the reciprocity identity used in Sec. 1.3.2.

A.3.1 Flux written in terms of the vector potential

Let the receive coil be a thin wire loop with path $\mathcal{C}$, and let $\vec{r}_c$ parameterize points along the coil with differential element $d\vec{\ell}_c$. The magnetization distribution $\vec{M}(\vec{r}, t)$ is confined to some volume $V_{\text{particles}}$.

The magnetic flux through the receive coil can be written as

$$\Phi(t) = \int_S \vec{B}(\vec{r}, t) \cdot d\vec{S} = \oint_{\mathcal{C}} \vec{A}(\vec{r}_c, t) \cdot d\vec{\ell}_c, \quad (\text{A.17})$$

where $\vec{A}$ is the vector potential ($\vec{B} = \nabla \times \vec{A}$) and the equality follows from Stokes' theorem.

In magnetostatics, a magnetization distribution can be represented by the equivalent bound current density

$$\vec{J}_b(\vec{r}, t) = \nabla \times \vec{M}(\vec{r}, t). \quad (\text{A.18})$$

The corresponding vector potential at a field point $\vec{r}_c$ is

$$\vec{A}(\vec{r}_c, t) = \frac{\mu_0}{4\pi} \int_{V_{\text{particles}}} \frac{\vec{J}_b(\vec{r}, t)}{|\vec{r}_c - \vec{r}|} dV. \quad (\text{A.19})$$

Substituting into the flux expression gives

$$\Phi(t) = \frac{\mu_0}{4\pi} \oint_{\mathcal{C}} \left[\int_{V_{\text{particles}}} \frac{\vec{J}_b(\vec{r}, t)}{|\vec{r}_c - \vec{r}|} dV \right] \cdot d\vec{\ell}_c. \quad (\text{A.20})$$

Interchanging the order of integration yields

$$\Phi(t) = \frac{\mu_0}{4\pi} \int_{V_{\text{particles}}} \vec{J}_b(\vec{r}, t) \cdot \left[\oint_{\mathcal{C}} \frac{d\vec{\ell}_c}{|\vec{r}_c - \vec{r}|} \right] dV. \quad (\text{A.21})$$

A.3.2 Removing the curl on $\vec{M}$

Using $\vec{J}_b = \nabla \times \vec{M}$ and the vector identity

$$(\nabla \times \vec{M}) \cdot \vec{F} = \nabla \cdot (\vec{M} \times \vec{F}) + \vec{M} \cdot (\nabla \times \vec{F}), \quad (\text{A.22})$$

with $\vec{F}(\vec{r}) = \oint_{\mathcal{C}} \frac{d\vec{\ell}_c}{|\vec{r}_c - \vec{r}|}$, we obtain

$$\Phi(t) = \frac{\mu_0}{4\pi} \int_{V_{\text{particles}}} \left[\nabla \cdot (\vec{M}(\vec{r}, t) \times \vec{F}(\vec{r})) + \vec{M}(\vec{r}, t) \cdot (\nabla \times \vec{F}(\vec{r})) \right] dV. \quad (\text{A.23})$$

The first term becomes a surface integral by the divergence theorem. Since $\vec{M}$ is confined to $V_{\text{particles}}$ (and vanishes outside), this surface term is zero. Therefore,

$$\Phi(t) = \frac{\mu_0}{4\pi} \int_{V_{\text{particles}}} \vec{M}(\vec{r}, t) \cdot (\nabla \times \vec{F}(\vec{r})) dV. \quad (\text{A.24})$$

A.3.3 Identification of the receive-coil sensitivity field

Because the curl operator acts on $\vec{r}$, it may be taken inside the line integral:

$$\nabla \times \vec{F}(\vec{r}) = \nabla \times \oint_{\mathcal{C}} \frac{d\vec{\ell}_c}{|\vec{r}_c - \vec{r}|} = \oint_{\mathcal{C}} \nabla \times \left(\frac{d\vec{\ell}_c}{|\vec{r} - \vec{r}_c|} \right). \quad (\text{A.25})$$

Using $\nabla \times (f d\vec{\ell}_c) = \nabla f \times d\vec{\ell}_c$ (with $d\vec{\ell}_c$ independent of $\vec{r}$) and $\nabla \left(\frac{1}{|\vec{r} - \vec{r}_c|} \right) = -\frac{\vec{r} - \vec{r}_c}{|\vec{r} - \vec{r}_c|^3}$ gives

$$\nabla \times \vec{F}(\vec{r}) = \oint_{\mathcal{C}} \left[-\frac{\vec{r} - \vec{r}_c}{|\vec{r} - \vec{r}_c|^3} \times d\vec{\ell}_c \right] = \oint_{\mathcal{C}} \frac{d\vec{\ell}_c \times (\vec{r} - \vec{r}_c)}{|\vec{r} - \vec{r}_c|^3}. \quad (\text{A.26})$$

Define the receive-coil sensitivity field $\vec{P}^R(\vec{r})$ as the magnetic field intensity produced at position $\vec{r}$ when the receive coil is driven with unit current. For a thin-wire loop, the Biot–Savart law gives

$$\vec{P}^R(\vec{r}) = \frac{1}{4\pi} \oint_{\mathcal{C}} \frac{d\vec{\ell}_c \times (\vec{r} - \vec{r}_c)}{|\vec{r} - \vec{r}_c|^3}. \quad (\text{A.27})$$

Substituting this into the flux expression yields the reciprocity identity

$$\Phi(t) = \mu_0 \int_{V_{\text{particles}}} \vec{P}^R(\vec{r}) \cdot \vec{M}(\vec{r}, t) dV. \quad (\text{A.28})$$

Finally, applying Faraday’s law $u(t) = -d\Phi/dt$ and noting that $\vec{P}^R(\vec{r})$ is time independent gives

$$u(t) = -\mu_0 \frac{d}{dt} \int_{V_{\text{particles}}} \vec{P}^R(\vec{r}) \cdot \vec{M}(\vec{r}, t) dV = -\mu_0 \int_{V_{\text{particles}}} \vec{P}^R(\vec{r}) \cdot \frac{\partial \vec{M}(\vec{r}, t)}{\partial t} dV, \quad (\text{A.29})$$

which is the form used in Sec. 1.3.2.

A.4 Proof of Odd Harmonics

The presence of only odd harmonics (at zero DC offset) in the MPI signal originates from the nonlinear magnetization response of SPIO to an applied magnetic field. This can be understood by examining the Langevin function and its response to a sinusoidal excitation.

The Taylor series expansion of the Langevin function is

$$\mathcal{L}(\xi) = \frac{1}{3}\xi - \frac{1}{45}\xi^3 + \frac{2}{945}\xi^5 - \frac{1}{4725}\xi^7 + \dots, \quad (\text{A.30})$$

which contains only odd powers of its argument. This reflects the fact that the Langevin function is an odd function, i.e. $\mathcal{L}(-\xi) = -\mathcal{L}(\xi)$.

In MPI, the argument of the Langevin function is proportional to the applied magnetic field. For a purely sinusoidal excitation field of angular frequency ω_D , the time-dependent argument (ξ) may be written (up to a constant scaling factor) as

$\xi(t) \propto \cos(\omega_D t)$. Substituting this into the series expansion gives

$$\mathcal{L}(\cos(\omega_D t)) = \frac{1}{3} \cos(\omega_D t) - \frac{1}{45} \cos^3(\omega_D t) + \frac{2}{945} \cos^5(\omega_D t) - \frac{1}{4725} \cos^7(\omega_D t) + \dots \quad (\text{A.31})$$

Using standard trigonometric identities, odd powers of cosine can be expressed as sums of cosines at odd multiples of the fundamental frequency, for example,

$$\cos^3(x) = \frac{1}{4} (3 \cos x + \cos 3x). \quad (\text{A.32})$$

More generally, $\cos^{2n+1}(x)$ expands into a linear combination of $\cos[(2k+1)x]$ terms only.

As a result, the magnetization response can be written as

$$\mathcal{L}(\cos(\omega_D t)) = A_1 \cos(\omega_D t) + A_2 \cos(3\omega_D t) + A_3 \cos(5\omega_D t) + A_4 \cos(7\omega_D t) + \dots, \quad (\text{A.33})$$

where A_i are time-independent coefficients. Thus the signal from the sample will contribute odd multiples of the fundamental frequency applied to the sample by the excitation.

APPENDIX B
CODE

B.1 Biot–Savart Field Simulation

Listing 2.1: MATLAB script used to compute magnetic field maps for selection, excitation, and receive coils using the Biot–Savart law.

```
1 %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
2 %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
3 %%      Biot Savart Simulation for FFL MPI Single-Sided Scanner  %%
4 %%      University of Massachusetts Boston                      %%
5 %%      Author: Christopher McDonough                          %%
6 %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
7 %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
8
9 %This program performs a numerical aproximation of the biot savart law to
10 %calculate the magnetic field over a certain volume
11
12 %You must specify the range you want the magnetic field calculated over
13 %You must specify the name you want your magnetic fields saved as
14 %You must specify the geometry of your coil
15
16 %Everything is assumed to be in SI units
17 %so enter distances in meters
18
19
20 %% Initialize the Program
21 %Here Iintialize the program nothing needs to be changed here
22
23 clear all
24
25 %% Define the range of your magnetic fields
26 %This is where you define the dimensions the magnetic field is over
27
```

```

28 %This is where you define the x range
29 start_x = -0/1000;
30 x_step = 1/1000;
31 end_x = 0/1000;
32
33 %This is where you define the y range
34 start_y = -0/1000;
35 y_step = 1/1000;
36 end_y = 0/1000;
37
38 %This is where you define the z range
39 start_z = 20/1000;
40 z_step = 0.5/1000;
41 end_z = 20/1000;
42
43 %% Define the name of your fields
44 %This is where you define the name of your field
45 %This will define how the script will name your fields
46
47 field_name = 'spiral';
48
49 %% Define Coil Geometry (Spiral for demonstration)
50
51 % User-defined parameters
52 R_max = 80./1000;      % Outer radius [m]
53 nTurns = 50;          % Number of spiral turns
54 N = 10000;            % Number of points
55
56 % Derived parameters
57 theta_max = 2*pi*nTurns;
58 b = R_max / theta_max;

```



```

59
60 % Parameter
61 theta = linspace(0, theta_max, N);
62
63 % Radius
64 r = b.*theta;
65
66 % Convert to Cartesian coordinates
67 x_coil = r.*cos(theta);
68 y_coil = r.*sin(theta);
69
70 z_coil = 0.*x_coil; % Coil located on surface of scanner
71
72 %%
73 %Here I plot the detector along with the coil geometry so you can know if
74 %your all of your inputs are correct
75
76 x_range = start_x:x_step:end_x;
77 y_range = start_y:y_step:end_y;
78 z_range = start_z:z_step:end_z;
79
80 figure(1);
81
82 PlotBiotSavart(x_coil,y_coil,z_coil,x_range,y_range,z_range);
83 axis('equal');
84
85
86 %%
87 %Here I define the physical constants present in the Biot Savart Law
88 mu_0 = 1.256637*10^(-6);
89 I = 1.0;

```

```

90 const = mu_0*I/(4*pi());
91
92 %% Ensure column vectors (defensive reshaping)
93
94 x_coil = x_coil(:);
95 y_coil = y_coil(:);
96 z_coil = z_coil(:);
97
98 %%
99 %Here is where the coil positions are manipulated to create dl
100
101 n_pt_coil = length(x_coil);
102
103 r_coil = [x_coil,y_coil,z_coil];
104
105 dl = zeros(n_pt_coil,3);
106
107 for i = 1:n_pt_coil
108
109     if i < n_pt_coil
110
111         dl(i,:) = r_coil(i+1,:) - r_coil(i,:);
112
113     else
114
115         dl(i,:) = r_coil(i,:) - r_coil(i-1,:);
116
117     end
118
119 end
120

```

```

121 %%
122 %This is where the Biot-Savart law is calculated
123
124 %Intialize Magnetic field
125 number_of_x = round(((end_x-start_x)./x_step)+1);
126 number_of_y = round(((end_y-start_y)./y_step)+1);
127 number_of_z = round(((end_z-start_z)./z_step)+1);
128
129 Bx = ones(number_of_x,number_of_y,number_of_z);
130 By = ones(number_of_x,number_of_y,number_of_z);
131 Bz = ones(number_of_x,number_of_y,number_of_z);
132
133 for x = x_range
134     x_index = round(((x-start_x)/x_step)+1);
135     for y = y_range
136         y_index = round(((y-start_y)/y_step)+1);
137         for z = z_range
138             z_index = round(((z-start_z)/z_step)+1);
139
140
141             %The sum term in the Biot Savart Law
142             sum = 0;
143
144             r = [x,y,z];
145
146             for pt_in_coil = 1:n_pt_coil
147
148                 r_dif = r - r_coil(pt_in_coil,:);
149
150                 integrand = cross(dl(pt_in_coil,:),r_dif)./((norm(r_dif)).^3);
151

```

```

152         sum = sum + integrand;
153
154     end
155
156     Bx(x_index,y_index,z_index) = const*sum(1);
157     By(x_index,y_index,z_index) = const*sum(2);
158     Bz(x_index,y_index,z_index) = const*sum(3);
159
160 end
161 end
162 end
163
164 %% Save Fields to Folder
165
166 Bx_name = strcat('Bx_',field_name);
167 By_name = strcat('By_',field_name);
168 Bz_name = strcat('Bz_',field_name);
169
170 cd Fields
171
172 save(Bx_name,'Bx');
173 save(By_name,'By');
174 save(Bz_name,'Bz');
175
176 cd ../
177
178 %% Subfunction for Ploting
179
180 function PlotBiotSavart(x_coil,y_coil,z_coil,x_range,y_range,z_range)
181
182 detector_length = 390/1000;

```

```

183 detector_height = 68.6/1000;
184 detector_width = 180/1000;
185
186 x1 = -detector_width/2;
187 x2 =detector_width/2;
188
189 y1 = -detector_length/2;
190 y2 = detector_length/2;
191
192 z1 = 0;
193 z2 = -detector_height;
194
195 step = 10/1000;
196
197 wall_color = 'black';
198 wall_trans = 0.05;
199
200 Wire_Color = [.722 .451 .2];
201
202 hold on
203
204 plot3(x_coil,y_coil,z_coil,'Color',Wire_Color);
205
206 [X_range,Y_range,Z_range] = meshgrid(x_range,y_range,z_range);
207
208 scatter3(X_range(:),Y_range(:),Z_range(:),'black','.');
209
210 fill3([x1 x2 x2 x1],[y1 y1 y2 y2],[z1 z1 z1 z1],wall_color,'FaceAlpha',wall_trans);
211 fill3([x1 x2 x2 x1],[y1 y1 y2 y2],[z2 z2 z2 z2],wall_color,'FaceAlpha',wall_trans);
212 fill3([x1 x1 x1 x1],[y1 y2 y2 y1],[z1 z1 z2 z2],wall_color,'FaceAlpha',wall_trans);
213 fill3([x2 x2 x2 x2],[y1 y2 y2 y1],[z1 z1 z2 z2],wall_color,'FaceAlpha',wall_trans);

```

```

214 fill3([x1 x2 x2 x1],[y1 y1 y1 y1],[z1 z1 z2 z2],wall_color,'FaceAlpha',wall_trans);
215 fill3([x1 x2 x2 x1],[y2 y2 y2 y2],[z1 z1 z2 z2],wall_color,'FaceAlpha',wall_trans);
216
217 hold off
218
219 end

```

B.2 Signal Detection Simulation

Listing 2.2: MATLAB script implementing the SPIO signal detection model, including Langevin magnetization dynamics and receive coil signal calculation.

```

1
2 function [tot_signal, M, signals] = simulate_detection( ...
3     beta, dt, ...
4     Bx_tot, By_tot, Bz_tot, ...
5     Px_rx, Py_rx, Pz_rx)
6
7 % SIMULATE_DETECTION
8 %   Simulates SPIO excitation and the corresponding receive-coil detection
9 %   generated by multiple SPIO voxels. The signal pathway is:
10 %       1. Magnetic field applied to each SPIO voxel (sum of excitation and selection fields)
11 %       2. Magnetization induced in each SPIO voxel (Langevin model)
12 %       3. Time derivative of magnetization (dM/dt), which induces voltage
13 %       4. Projection of dM/dt onto the receive-coil sensitivity profiles
14 %       5. Summation of contributions from all SPIO voxels
15 %
16 %   INPUTS:
17 %       beta    - SPIO Langevin scaling factor (depends on SPIO size/material/temperature)
18 %       dt      - time difference
19 %       Bx_tot  - total applied magnetic field (x-component) at each voxel and time step
20 %       By_tot  - total applied magnetic field (y-component)

```

```

21 %      Bz_tot - total applied magnetic field (z-component)
22 %      Px_rx - receive-coil sensitivity profile in the x-direction
23 %      Py_rx - receive-coil sensitivity profile in the y-direction
24 %      Pz_rx - receive-coil sensitivity profile in the z-direction
25 %
26 %  OUTPUT:
27 %      tot_signal - 1xT simulated receive-coil voltage time series
28 %      M          - (optional) SPIO magnetization values per voxel and time
29 %      signals    - (optional) induced voltage per voxel and time
30 %
31 %  ASSUMPTIONS:
32 %      - Fields must be formatted correctly: SPIO voxel index along dimension 1,
33 %        time along dimension 2.
34 %      - gradient(...) computes dM/dt assuming uniform time steps
35 %      - Px_rx, Py_rx, and Pz_rx match the voxel layout of the SPIO distribution
36 %
37 %  This function provides a simplified but physically consistent model of MPI
38 %  signal formation for higher level simulations.
39
40
41 % Compute the magnitude of the total magnetic field at each SPIO voxel
42 B_tot_mod = sqrt(Bx_tot.^2 + By_tot.^2 + Bz_tot.^2);
43
44 % Compute the directional unit-vector components of the magnetic field
45 [x_dir,y_dir,z_dir] = CalcDirectionVector(Bx_tot,By_tot,Bz_tot,B_tot_mod);
46
47 % Compute the dimensionless Langevin parameter (beta encodes SPIO properties)
48 etta = beta.*B_tot_mod;
49
50 % Compute the magnetization using the Langevin function
51 M = Langevin(etta);

```

```

52
53 % Resolve the magnetization vector into x, y, and z components
54 Mx = x_dir.*M;
55 My = y_dir.*M;
56 Mz = z_dir.*M;
57
58 % Numerically compute the time derivative of the magnetization components
59 % Note: gradient(Mx) returns dMx/dt along dimension 1 assuming uniform time steps
60 dMx_dt = gradient(Mx)./dt;
61 dMy_dt = gradient(My)./dt;
62 dMz_dt = gradient(Mz)./dt;
63
64 % Use nargin to avoid allocating a full 'signals' matrix unless requested
65 if nargin < 3
66     % Most common: user only wants total signal
67     % Combine voxel voltage contributions and sum directly
68     tot_signal = sum(dMx_dt.*Px_rx + dMy_dt.*Py_rx + dMz_dt.*Pz_rx, 1);
69 else
70     % Compute the induced voltage contribution from each SPI0 voxel
71     % using the receive coil sensitivity profiles (Px_rx, Py_rx, Pz_rx)
72     signals = dMx_dt.*Px_rx + dMy_dt.*Py_rx + dMz_dt.*Pz_rx;
73
74     % Sum the contributions from all SPI0 voxels.
75     % In a real MPI system, the receive coil measures only the aggregate signal.
76     tot_signal = sum(signals, 1);
77 end
78
79 end

```

B.3 One-Dimensional Projection Imaging Simulation

Listing 2.3: MATLAB script used to simulate one-dimensional projection imaging by scanning the FFL laterally and extracting the third harmonic receive signal.

```

1 function [proj_1D, rx_signal_last, M_last, signals_last] = simulate_1D_projection( ...
2     beta, dt, t, f_1, n_harm, ...
3     B_ex_x, B_ex_y, B_ex_z, ...
4     Px_1, Py_1, Pz_1, ...
5     Px_2, Py_2, Pz_2, ...
6     I1s, I2s, ...
7     Px_rx, Py_rx, Pz_rx)
8 % SIMULATE_1D_PROJECTION
9 %
10 %   Compute a 1D MPI projection by scanning the Field-Free Line (FFL)
11 %   along x using precomputed excitation fields and selection/receive
12 %   field maps evaluated at SPIO locations.
13 %
14 %   For each FFL position:
15 %       - Selection coil currents (I1, I2) are applied
16 %       - The static selection field is computed at each SPIO
17 %       - The total field  $B(t) = B_{exc}(t) + B_{sel}$  is formed
18 %       - The receive signal is simulated using a Langevin-based model
19 %       - The specified harmonic is extracted via lock-in detection
20 %       - The harmonic amplitude is stored as one element of the projection
21 %
22 % INPUTS:
23 %   beta      - Langevin scaling parameter [1/T]
24 %   dt        - Time step [s]
25 %   t         - Time vector over one excitation period [s]
26 %   f_1       - Excitation frequency [Hz]
27 %   harmonic  - Harmonic number to extract (e.g., 3)
28 %

```

```

29 % B_ex_x/y/z - Excitation field components at SPI0 locations vs time [T]
30 %
31 % Px_1/y/z - Selection coil 1 field per amp at SPI0 locations [T/A]
32 % Px_2/y/z - Selection coil 2 field per amp at SPI0 locations [T/A]
33 %
34 % I1s, I2s - Selection coil currents for each FFL position [A]
35 %
36 % Px_rx/y/z - Receive coil sensitivity components at SPI0 locations [T/A]
37 %
38 % OUTPUTS:
39 % proj_1D - 1D projection (harmonic amplitude vs FFL position)
40 % rx_signal_last - Receive signal from final FFL position (debug)
41 % M_last - Magnetization from final FFL position (debug)
42 % signals_last - Intermediate signals from final FFL position (debug)
43 %
44 % NOTES:
45 % - Field arrays must be dimensionally compatible for broadcasting.
46 % - dt must be scalar (use dt = t(2)-t(1)).
47 % - No normalization is applied inside this function.
48
49 % -----
50 % Basic validation
51 % -----
52
53 if length(I1s) ~= length(I2s)
54     error('I1s and I2s must have the same length.');

```

```

60
61     % -----
62     % Initialize outputs
63     % -----
64     N_ffl = length(I1s);
65     proj_1D = zeros(N_ffl,1);
66
67     rx_signal_last = [];
68     M_last = [];
69     signals_last = [];
70
71     % -----
72     % FFL scan loop
73     % -----
74     for i = 1:N_ffl
75
76         I1 = I1s(i);           % Selection coil 1 current [A]
77         I2 = I2s(i);           % Selection coil 2 current [A]
78
79         % Static selection field at SPIO locations
80         B_sel_x = I1.*Px_1 + I2.*Px_2;
81         B_sel_y = I1.*Py_1 + I2.*Py_2;
82         B_sel_z = I1.*Pz_1 + I2.*Pz_2;
83
84         % Total applied field at SPIO locations
85         Bx_tot = B_ex_x + B_sel_x;
86         By_tot = B_ex_y + B_sel_y;
87         Bz_tot = B_ex_z + B_sel_z;
88
89         % Simulate receive signal
90         [rx_signal, M, signals] = simulate_detection( ...

```

```

91         beta, dt, Bx_tot, By_tot, Bz_tot, Px_rx, Py_rx, Pz_rx);
92
93     % Lock-in extraction of desired harmonic
94     [~, b_h] = lock_in_amp(t, rx_signal, f_1, n_harm);
95
96     % Store harmonic amplitude
97     proj_1D(i) = b_h;
98
99     % Store last-iteration outputs (useful for debugging)
100    rx_signal_last = rx_signal;
101    M_last = M;
102    signals_last = signals;
103
104    end
105 end

```

B.4 Two-Dimensional XY Tomographic Imaging Simulation

Listing 2.4: MATLAB script used to simulate two-dimensional XY tomographic imaging by rotating the phantom, acquiring multiple 1D projections, and reconstructing images using filtered backprojection.

```

1 % -----
2 % Script: XY_imaging
3 %
4 % Purpose:
5 %   Simulate 2D ( xy ) MPI imaging using a single-sided Field-Free-Line (FFL)
6 %   scanner by acquiring a set of 1D projections and reconstructing them
7 %   using filtered backprojection (FBP).
8 %
9 %   The script performs the following steps:
10 %       - Load precomputed 3D magnetic field maps for:

```

```

11 %      * selection coils (static encoding / FFL positioning)
12 %      * excitation (drive) coil (time-varying field)
13 %      * receive coil (sensitivity for signal detection)
14 %      - Define a fixed SPIO phantom in the xy plane at a constant height z
15 %      - Rotate the phantom through multiple angles to emulate Radon sampling
16 %      - For each rotation angle:
17 %          * Scan the FFL along x by adjusting selection coil currents
18 %          * Compute total applied field at SPIO locations
19 %          * Simulate receive signal using a Langevin-based model
20 %          * Extract the 3rd harmonic amplitude via lock-in detection
21 %          * Store the result as one column of a sinogram
22 %      - Reconstruct a 2D image using iradon()
23 %      - Plot the sinogram, reconstructed image, and ground-truth phantom
24 %
25 % -----
26
27 clear all          % Clear workspace variables
28 close all         % Close all open figure windows
29
30 originalFolder = pwd;      % Store original working directory
31 subscriptFolder = "Subscripts"; % Folder containing helper functions
32
33 %% Calculate beta
34 % beta is the Langevin scaling parameter governing SPIO magnetization.
35 % It can be modeled but here it is calculated from data of SynomagD
36
37 FWHM = 4.4/1000;    % Full Width at Half Maximum of particle response [T]
38 beta = 4.16./FWHM; % Empirical conversion from FWHM to beta [1/T]
39
40 %% Physical Scaling Factor (currently unused)
41 % Placeholder for absolute signal scaling (e.g., particle concentration,

```

```

42 % magnetic moment, voxel volume). Currently not applied so results are
43 % normalized and reported in arbitrary units.
44
45 % c = 1;           % concentration scaling (placeholder)
46 % m = 1;           % magnetic moment scaling (placeholder)
47 % dV = 1;          % voxel volume element (placeholder)
48 % scaling_factor = c.*m.*dV; % overall scaling (unused)
49
50 %% Load Fields
51 % Load precomputed 3D magnetic field maps (per 1 A current) for:
52 %   - Two selection coils (used to generate and shift the FFL)
53 %   - One excitation (drive) coil
54 %   - One receive coil (sensitivity map used for signal projection)
55 %
56 % NOTE:
57 %   Field maps are defined on a regular (X, Y, Z) grid. This requires careful
58 %   handling during interpolation (see interp3 calls below).
59
60 fieldFolder = 'Fields';
61 cd(fieldFolder); % Move into folder containing the .mat field maps
62
63 % Grid points where the fields are defined (must match the .mat map dimensions/order)
64 X_fields = -20:20; % x grid for simulated fields [mm]
65 Y_fields = -20:20; % y grid for simulated fields [mm]
66 Z_fields = 10:0.5:20; % z grid for simulated fields [mm]
67
68 % Selection coil 1 field maps (per 1 A current)
69 P_1_x_full = (load('Bx_selc1.mat')).Bx; % Bx at 1 A [T/A]
70 P_1_y_full = (load('By_selc1.mat')).By; % By at 1 A [T/A]
71 P_1_z_full = (load('Bz_selc1.mat')).Bz; % Bz at 1 A [T/A]
72

```

```

73 % Selection coil 2 field maps (per 1 A current)
74 P_2_x_full = (load('Bx_selc2.mat').Bx); % Bx at 1 A [T/A]
75 P_2_y_full = (load('By_selc2.mat').By); % By at 1 A [T/A]
76 P_2_z_full = (load('Bz_selc2.mat').Bz); % Bz at 1 A [T/A]
77
78 % Excitation/drive coil field maps (per 1 A current)
79 P_ex_x_full = (load('Bx_selc3.mat').Bx); % Bx at 1 A [T/A]
80 P_ex_y_full = (load('By_selc3.mat').By); % By at 1 A [T/A]
81 P_ex_z_full = (load('Bz_selc3.mat').Bz); % Bz at 1 A [T/A]
82
83 % Receive coil sensitivity (or receive field map) used for signal projection
84 B_rx_x_full = (load('Bx_rx.mat').Bx); % Rx sensitivity map x-component [T/A]
85 B_rx_y_full = (load('By_rx.mat').By); % Rx sensitivity map y-component [T/A]
86 B_rx_z_full = (load('Bz_rx.mat').Bz); % Rx sensitivity map z-component [T/A]
87
88 % Return to the original working directory, then go to the scripts folder
89 cd(originalFolder);
90 cd(subscriptFolder);
91
92 %% Calculate selection coil currents
93 % Compute the pair of selection coil currents required to shift the FFL
94 % along the x-direction. The scan coordinate X_ffl defines the FFL position(s).
95
96 X_ffl = -20:1:20; % FFL scan positions along x [mm]
97 I0 = 110; % Total current I0 = I1 + I2 (determines gradient) [A]
98
99 [I1s,I2s] = Calc_Selc_Currents_2Coil(X_ffl,I0,120,0);
100 N_ffl = length(X_ffl); % Number of FFL positions in the scan
101
102
103 %% Define SPI0 geometry

```

```

104 % Define fixed SPIO locations in space.
105
106 % N_SPIO = 21;           % Number of SPIOs per vertical line
107
108 % Define SPIO coordinates (here: a line along y from -10 to 10 mm at x=0, z=17.2)
109 % x_SPIO = [-10];
110 % y_SPIO = [-10];
111 % N_SPIO = length(x_SPIO);
112 % z_SPIO = zeros(N_SPIO,1)+17.2;
113
114 % --- Two-point asymmetric phantom ---
115 x_SPIO = [-6; 10];
116 y_SPIO = [ 4; -3];
117 z_SPIO = 17.2 * ones(2,1);
118
119
120 % Ensure column vectors (defensive reshaping) (if omitted script will break)
121 x_SPIO = x_SPIO(:);
122 y_SPIO = y_SPIO(:);
123 z_SPIO = z_SPIO(:);
124
125 %% Excitation Field Parameters
126 % Define the sinusoidal excitation waveform. The excitation field at each
127 % SPIO location is obtained by scaling the per-amp field maps by the
128 % excitation current.
129
130 N_t = 100;           % Number of samples per excitation period
131 f_1 = 25000;         % Excitation frequency [Hz]
132 w_1 = 2*pi*f_1;      % Angular frequency [rad/s]
133 t    = linspace(0,1/f_1,N_t);
134 dt   = t(2) - t(1);  % Time step [s]

```



```

135
136 I_ex_peak = 70;          % Peak drive current [A]
137 I_ex = I_ex_peak*cos(w_1*t);
138
139
140 %% Rotate SPI0 phantom (Radon-style acquisition)
141 % Multiple projection angles are generated by rotating the phantom about
142 % the origin in the xy plane. For each angle, a full 1D FFL scan is
143 % performed, producing one column of the sinogram.
144
145 N_ang = 20;              % Number of projection angles
146 angles_degrees = linspace(0,180,N_ang+1);
147 angles_degrees(end) = []; % Remove redundant 180 angle
148 angles_radians = pi*angles_degrees/180;
149
150 sinogram = zeros(N_ffl,N_ang); % Rows: FFL position, Columns: angle index
151
152
153 for i = 1:N_ang
154
155     angle_now = angles_radians(i);
156
157     x_SPI0_rot = x_SPI0.*cos(angle_now)-y_SPI0.*sin(angle_now);
158     y_SPI0_rot = x_SPI0.*sin(angle_now)+y_SPI0.*cos(angle_now);
159
160 %% Interpolate fields at rotated SPI0 positions
161 % interp3 is intentionally called with swapped grid vectors and query
162 % coordinates to match MATLABs handling of vector grids and the way field
163 % maps are stored. This is correct and verified.
164
165 % Interpolate selection coil 1 field components onto SPI0 points

```

```

166 Px_1 = interp3(Y_fields, X_fields, Z_fields, P_1_x_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
167 Py_1 = interp3(Y_fields, X_fields, Z_fields, P_1_y_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
168 Pz_1 = interp3(Y_fields, X_fields, Z_fields, P_1_z_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
169
170 % Interpolate selection coil 2 field components onto SPI0 points
171 Px_2 = interp3(Y_fields, X_fields, Z_fields, P_2_x_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
172 Py_2 = interp3(Y_fields, X_fields, Z_fields, P_2_y_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
173 Pz_2 = interp3(Y_fields, X_fields, Z_fields, P_2_z_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
174
175 % Interpolate excitation/drive coil field components onto SPI0 points
176 Px_ex = interp3(Y_fields, X_fields, Z_fields, P_ex_x_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
177 Py_ex = interp3(Y_fields, X_fields, Z_fields, P_ex_y_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
178 Pz_ex = interp3(Y_fields, X_fields, Z_fields, P_ex_z_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
179
180 % Interpolate receive coil sensitivity components onto SPI0 points
181 Px_rx = interp3(Y_fields, X_fields, Z_fields, B_rx_x_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
182 Py_rx = interp3(Y_fields, X_fields, Z_fields, B_rx_y_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
183 Pz_rx = interp3(Y_fields, X_fields, Z_fields, B_rx_z_full, y_SPI0_rot, x_SPI0_rot, z_SPI0);
184
185 % Calculate excitation field by multiplying
186 B_ex_x = I_ex.*Px_ex; % Excitation field x-component at each SPI0 location vs time
187 B_ex_y = I_ex.*Py_ex; % Excitation field y-component at each SPI0 location vs time
188 B_ex_z = I_ex.*Pz_ex; % Excitation field z-component at each SPI0 location vs time
189
190 %% Simulate 1D projection
191
192 proj_1D = simulate_1D_projection( ...
193     beta, dt, t, f_1, 3, ...
194     B_ex_x, B_ex_y, B_ex_z, ...
195     Px_1, Py_1, Pz_1, ...
196     Px_2, Py_2, Pz_2, ...

```

```

197     I1s, I2s, ...
198     Px_rx, Py_rx, Pz_rx);
199
200 sinogram(:,i) = proj_1D;
201
202 end
203
204 %% Plot Phantom (Ground Truth)
205 % Display the original (unrotated) SPIO phantom for comparison with the
206 % reconstructed image.
207
208 font_size = 23;
209
210 figure(1);
211 subplot(1,3,1);
212
213 scatter(x_SPIO,y_SPIO,'filled','k');
214 xlim([min(X_ffl) max(X_ffl)]);
215 ylim([min(X_ffl) max(X_ffl)]);
216 grid on
217 set(gca,'FontSize',font_size);
218 xticks([-20 -10 0 10 20]);
219 yticks([-20 -10 0 10 20]);
220 xlabel('X (mm)');
221 ylabel('Y (mm)');
222 axis('square');
223 title('(a)');
224
225
226 %% Plot Sinogram
227 % The sinogram represents harmonic amplitude as a function of:

```

```

228 % - Vertical axis: FFL x-position
229 % - Horizontal axis: projection angle
230
231 % figure(2);
232 subplot(1,3,2);
233
234 imagesc(angles_degrees,X_ffl,sinogram);
235 set(gca,'Ydir','normal');
236 xlabel('Angles (degrees)');
237 ylabel('X FFL (mm)');
238 set(gca,'FontSize',font_size);
239 axis('square');
240 title('(b)');
241
242
243 %% Reconstruct Image
244 % Perform filtered backprojection using MATLABs iradon().
245 % The sinogram is provided in detector-position angle format, which
246 % matches iradons expected input.
247
248 fbp_image = iradon(sinogram, angles_degrees, 'linear', 'Hann', 1.0,N_ffl);
249
250 % figure(3);
251 subplot(1,3,3);
252
253 imagesc(X_ffl,X_ffl,fbp_image);
254 set(gca,'Ydir','normal');
255 xlabel('X (mm)');
256 ylabel('Y (mm)');
257 axis('square');
258 set(gca,'FontSize',font_size);

```

```

259 xticks([-20 -10 0 10 20]);
260 title('(c)');
261
262
263 %% Return to Original Folder
264
265 cd(originalFolder);

```

B.5 Two-Dimensional XZ Projection Imaging Simulation

Listing 2.5: MATLAB script used to simulate two-dimensional XZ projection imaging by translating the phantom in height and stacking one-dimensional FFL projections.

```

1 % -----
2 % Script: XZ_imaging
3 %
4 % Purpose:
5 %   Simulate 2D ( xz ) MPI imaging our single-sided Field-Free-Line (FFL)
6 %   scanner by forming a set of 1D projections versus FFL x-position at
7 %   multiple phantom heights (z positions). The resulting data is arranged
8 %   into a 2D xz "projection image".
9 %
10 %   Conceptual workflow:
11 %       1) Load precomputed 3D coil field maps (per 1 A) for:
12 %           - selection coils (static selection field / FFL positioning)
13 %           - excitation coil (time-varying drive field)
14 %           - receive coil   (sensitivity weighting for detection)
15 %       2) Define an SPIO phantom location (x,y fixed; base z specified).
16 %       3) Define a set of z offsets (sample different heights of the phantom).
17 %       4) For each z offset:
18 %           - Interpolate coil fields to the SPIO location at that height
19 %           - For each FFL x-position:

```

```

20 %          * apply the corresponding selection currents (I1, I2)
21 %          * compute total field: B_total(t) = B_exc(t) + B_sel
22 %          * simulate receive signal via simulate_detection()
23 %          * extract 3rd harmonic amplitude via lock_in_amp()
24 %          * store amplitude at [x_index, z_index]
25 %      5) Plot:
26 %          - ground-truth phantom location in xz
27 %          - normalized xz amplitude map (projection image)
28 %
29 % -----
30
31 clear all          % Clear workspace variables
32 close all         % Close all open figure windows
33
34 originalFolder = pwd;          % Store original working directory
35 subscriptFolder = "Subscripts"; % Folder containing helper functions
36
37 %% Calculate beta
38 % beta is the Langevin scaling parameter governing SPIO magnetization
39 % nonlinearity. Here it is estimated from Synomag-D particle FWHM data.
40
41 FWHM = 4.4/1000; % Full Width at Half Maximum of particle response [T]
42 beta = 4.16./FWHM; % Empirical conversion from FWHM to beta [1/T]
43
44 %% Physical Scaling Factor (currently unused)
45 % Placeholder for absolute signal scaling (e.g., concentration, magnetic moment,
46 % voxel volume). Not applied here.
47
48 % c = 1;          % concentration scaling (placeholder)
49 % m = 1;          % magnetic moment scaling (placeholder)
50 % dV = 1;         % voxel volume element (placeholder)

```

```

51 % scaling_factor = c.*m.*dV; % overall scaling (unused)
52
53 %% Load Fields
54 % Load precomputed 3D magnetic field maps (per 1 A current)
55 %
56 % Field maps are defined on a regular grid: X_fields, Y_fields, Z_fields.
57 % Interpolation is performed later at the SPI0 coordinates.
58
59 fieldFolder = 'Fields';
60 cd(fieldFolder); % Move into folder containing the .mat field maps
61
62 % Grid points where the fields are defined (must match the .mat map dimensions/order)
63 X_fields = -20:20; % x grid for simulated fields [mm]
64 Y_fields = -20:20; % y grid for simulated fields [mm]
65 Z_fields = 10:0.5:20; % z grid for simulated fields [mm]
66
67 % Selection coil 1 field maps (per 1 A current)
68 P_1_x_full = (load('Bx_selc1.mat')).Bx); % Bx at 1 A [T/A]
69 P_1_y_full = (load('By_selc1.mat')).By); % By at 1 A [T/A]
70 P_1_z_full = (load('Bz_selc1.mat')).Bz); % Bz at 1 A [T/A]
71
72 % Selection coil 2 field maps (per 1 A current)
73 P_2_x_full = (load('Bx_selc2.mat')).Bx); % Bx at 1 A [T/A]
74 P_2_y_full = (load('By_selc2.mat')).By); % By at 1 A [T/A]
75 P_2_z_full = (load('Bz_selc2.mat')).Bz); % Bz at 1 A [T/A]
76
77 % Excitation/drive coil field maps (per 1 A current)
78 P_ex_x_full = (load('Bx_selc3.mat')).Bx); % Bx at 1 A [T/A]
79 P_ex_y_full = (load('By_selc3.mat')).By); % By at 1 A [T/A]
80 P_ex_z_full = (load('Bz_selc3.mat')).Bz); % Bz at 1 A [T/A]
81

```

```

82 % Receive coil sensitivity (or receive field map)
83 B_rx_x_full = (load('Bx_rx.mat')).Bx); % Rx sensitivity map x-component [T/A]
84 B_rx_y_full = (load('By_rx.mat')).By); % Rx sensitivity map y-component [T/A]
85 B_rx_z_full = (load('Bz_rx.mat')).Bz); % Rx sensitivity map z-component [T/A]
86
87 % Return to the original working directory, then go to the scripts folder
88 cd(originalFolder);
89 cd(subscriptFolder);
90
91 %% Calculate selection coil currents (FFL x-scan)
92 % X_ffl defines the desired FFL x-position for each scan step. The function
93 % Calc_Selc_Currents_2Coil computes the corresponding (I1, I2) values under
94 % the constraint  $I_1 + I_2 = I_0$ .
95
96 X_ffl = -20:1:20; % FFL scan positions along x [mm]
97 I0 = 110; % Total current  $I_0 = I_1 + I_2$  (determines gradient) [A]
98
99 [I1s,I2s] = Calc_Selc_Currents_2Coil(X_ffl,I0,120,0);
100 N_ffl = length(X_ffl); % Number of FFL positions in the scan
101
102 %% Define SPI0 geometry (phantom)
103 % Define the SPI0 location(s). In this script, the phantom is a single
104 % point at (x,y) = (0,0). The z location is swept by adding offsets.
105
106 x_SPI0 = [0]; % Phantom x [mm]
107 y_SPI0 = [0]; % Phantom y [mm]
108 N_SPI0 = length(x_SPI0);
109 z_SPI0 = zeros(N_SPI0,1) + 10; % Starting phantom height [mm]
110
111 % Ensure column vectors (defensive reshaping) (if omitted script could break)
112 x_SPI0 = x_SPI0(:);

```



```

113 y_SPI0 = y_SPI0(:);
114 z_SPI0 = z_SPI0(:);
115
116 %% Excitation Field Parameters
117 % Define the sinusoidal excitation waveform. The excitation field at each
118 % SPI0 location is obtained by scaling the per-amp field maps by the
119 % excitation current.
120
121 N_t = 100;           % Number of samples per excitation period
122 f_1 = 25000;         % Excitation frequency [Hz]
123 w_1 = 2*pi*f_1;      % Angular frequency [rad/s]
124 t   = linspace(0,1/f_1,N_t);
125 dt  = t(2) - t(1);   % Time step [s]
126
127 I_ex_peak = 7;        % Peak drive current [A]
128 I_ex = I_ex_peak*cos(w_1*t);
129
130 %% Sweep phantom height (z) to form an XZ projection image
131 % Sample N_z different z positions by shifting the phantom height by Z_offsets.
132 % For each height, we perform a full 1D FFL scan along x and store the
133 % extracted harmonic amplitude in proj_2D(x_index, z_index).
134
135 N_z = 21;             % Number of z samples
136 z_step = 0.5;         % z increment [mm]
137 Z_offsets = linspace(0,(N_z-1)*z_step,N_z);
138
139 proj_2D = zeros(N_ffl,N_z); % Rows: x scan index, Columns: z index
140
141 for i = 1:N_z
142
143     height_now = Z_offsets(i); % Current z offset [mm]

```

```

144     z_SPIO_new = z_SPIO + height_now; % Updated phantom height [mm]
145
146     %% Interpolate coil fields at the current phantom height
147
148     % Selection coil 1 fields at SPIO
149     Px_1 = interp3(Y_fields, X_fields, Z_fields, P_1_x_full, y_SPIO, x_SPIO, z_SPIO_new);
150     Py_1 = interp3(Y_fields, X_fields, Z_fields, P_1_y_full, y_SPIO, x_SPIO, z_SPIO_new);
151     Pz_1 = interp3(Y_fields, X_fields, Z_fields, P_1_z_full, y_SPIO, x_SPIO, z_SPIO_new);
152
153     % Selection coil 2 fields at SPIO
154     Px_2 = interp3(Y_fields, X_fields, Z_fields, P_2_x_full, y_SPIO, x_SPIO, z_SPIO_new);
155     Py_2 = interp3(Y_fields, X_fields, Z_fields, P_2_y_full, y_SPIO, x_SPIO, z_SPIO_new);
156     Pz_2 = interp3(Y_fields, X_fields, Z_fields, P_2_z_full, y_SPIO, x_SPIO, z_SPIO_new);
157
158     % Excitation/drive coil fields at SPIO
159     Px_ex = interp3(Y_fields, X_fields, Z_fields, P_ex_x_full, y_SPIO, x_SPIO, z_SPIO_new);
160     Py_ex = interp3(Y_fields, X_fields, Z_fields, P_ex_y_full, y_SPIO, x_SPIO, z_SPIO_new);
161     Pz_ex = interp3(Y_fields, X_fields, Z_fields, P_ex_z_full, y_SPIO, x_SPIO, z_SPIO_new);
162
163     % Receive coil sensitivity at SPIO
164     Px_rx = interp3(Y_fields, X_fields, Z_fields, B_rx_x_full, y_SPIO, x_SPIO, z_SPIO_new);
165     Py_rx = interp3(Y_fields, X_fields, Z_fields, B_rx_y_full, y_SPIO, x_SPIO, z_SPIO_new);
166     Pz_rx = interp3(Y_fields, X_fields, Z_fields, B_rx_z_full, y_SPIO, x_SPIO, z_SPIO_new);
167
168     % Calculate excitation field
169     B_ex_x = I_ex.*Px_ex; % Excitation field x-component vs time
170     B_ex_y = I_ex.*Py_ex; % Excitation field y-component vs time
171     B_ex_z = I_ex.*Pz_ex; % Excitation field z-component vs time
172
173     %% Simulate 1D projection
174

```

```

175     proj_1D = simulate_1D_projection( ...
176         beta, dt, t, f_1, 3, ...
177         B_ex_x, B_ex_y, B_ex_z, ...
178         Px_1, Py_1, Pz_1, ...
179         Px_2, Py_2, Pz_2, ...
180         I1s, I2s, ...
181         Px_rx, Py_rx, Pz_rx);
182
183 proj_2D(:,i) = proj_1D;
184
185 end
186
187 %% Plot phantom (ground truth) and XZ projection map
188 % Z_ffl is the displayed z-axis coordinate for the sampled heights. Here it
189 % is mapped as 17 - Z_offsets for plotting convenience relative to a
190 % reference height (adjust as needed for your coordinate system).
191
192 Z_plot = 17 - Z_offsets;
193
194 font_size = 23;
195
196 figure(1);
197 subplot(1,2,1);
198
199 % Ground-truth phantom location in xz (single point in this example)
200 scatter(x_SPI0, z_SPI0, 'filled', 'k');
201 axis equal;
202 xlim([min(X_ffl) max(X_ffl)]);
203 ylim([min(Z_plot) max(Z_plot)]);
204 grid on
205 set(gca, 'FontSize', font_size);

```

```

206 xticks([-20 -10 0 10 20]);
207 xlabel('X (mm)');
208 ylabel('Z (mm)'); % (y-axis is z in this plot)
209
210 title('(a)');
211
212 %% Plot the XZ projection image
213 % proj_2D is stored as [x_index, z_index], but imagesc maps matrix rows to
214 % the y-axis. Therefore transpose(proj_2D) is plotted so that:
215 % - x-axis corresponds to X_ffl
216 % - y-axis corresponds to Z_ffl
217 % The image is normalized to its maximum for display.
218
219 subplot(1,2,2);
220
221 imagesc(X_ffl, Z_plot, transpose(proj_2D)./max(max(proj_2D)));
222 set(gca,'Ydir','normal');
223 xlabel('X (mm)');
224 ylabel('Z (mm)');
225 set(gca,'FontSize',font_size);
226 axis equal;
227 ylim([min(Z_plot)-z_step/2, max(Z_plot)+z_step/2]);
228 colorbar;
229
230 title('(b)');
231
232 %% Return to Original Folder
233 cd(originalFolder);

```

B.6 LabVIEW Imager GUI

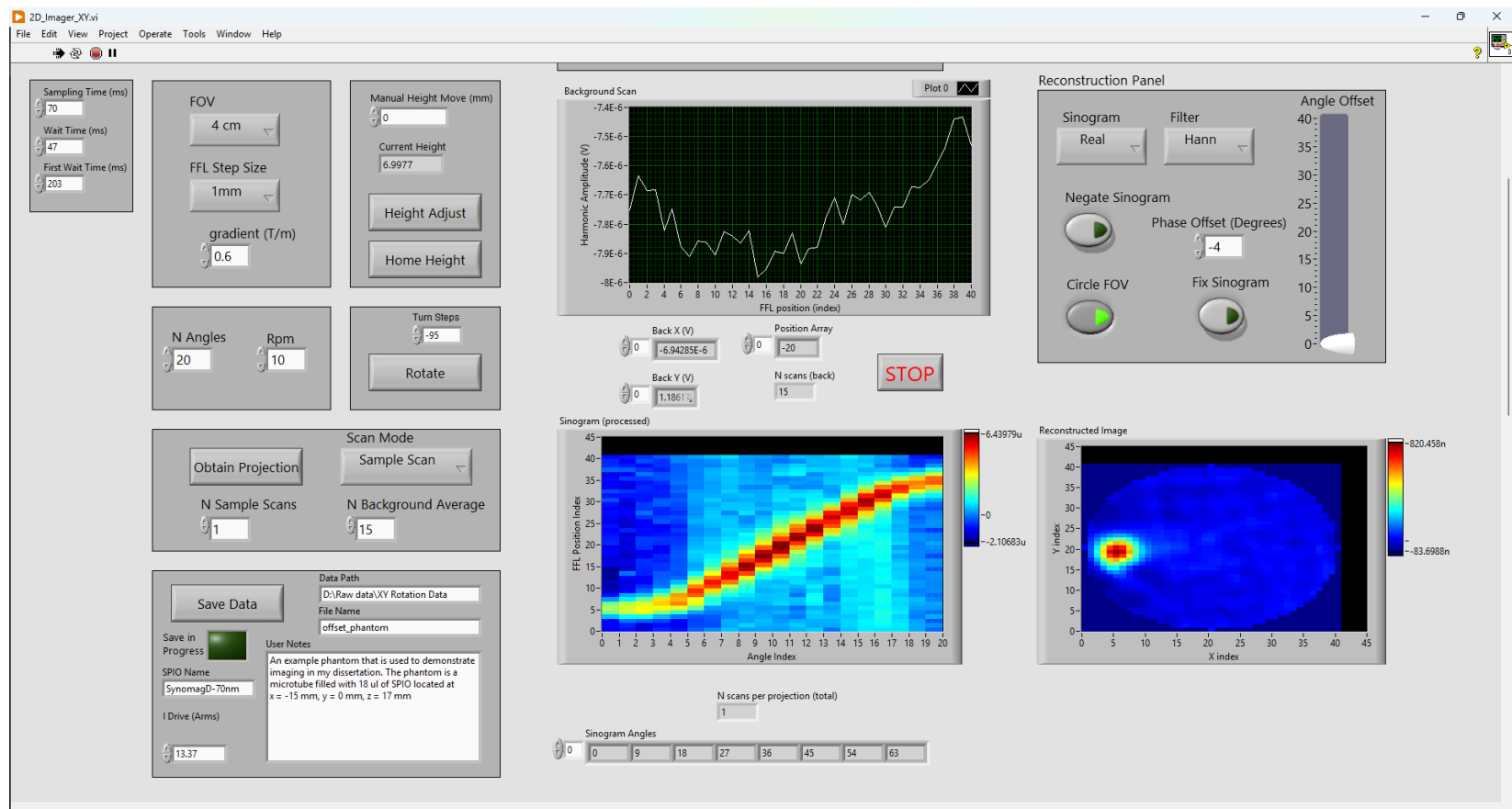


Figure B.1: LabVIEW front panel used for 2D image acquisition.

APPENDIX C
APPROVALS AND PERMISSIONS

From: eSirius3GWebServer no-reply@esirius.cayuse.com
Subject: Committee Action Record - New or De Novo IBC Protocol # IBC-00001081 Approval
Date: September 11, 2023 at 3:21 PM
To: tonyushkin@oakland.edu

E



Reference: IBC Protocol # IBC-00001081

Protocol Title: A Single-Sided Magnetic Particle Imaging Scanner for In Vivo Breast Cancer Imaging

Principal Investigator: Tonyushkin, Alexey

Approval Period: 09/11/2023 - 09/11/2026

Dear Professor Tonyushkin, Alexey:

The Institutional Biosafety Committee (IBC), responsible for the review of research involving materials of human origin, recombinant DNA, and biohazardous, infectious or toxic materials, has reviewed the original proposal, noted the revisions provided by you upon committee's request (if applicable), and approved the project referenced above. This is your formal approval notice; please save it for your records.

The proposed activities are approved for a period of three years, starting 09/11/2023 and ending 09/11/2026, and assigned the approval # IBC-00001081. Please be aware that protocols expire at 12:01 AM on the expiration date. The highest BSL level approved for the protocol can be found on the Overview page of the protocol form.

Any unanticipated problems, changes in, or halting of the activities proposed in the project, as described, must be promptly reported to the IBC or the biosafety officer.

In addition, all faculty, staff, and students involved in the project must be trained and qualified to conduct the project in a responsible manner. Please note, in this regard, that you, the Principal Investigator, are fully responsible at all times for limiting or restricting access to laboratories and for assessing, in each circumstance, who may enter or work in a laboratory when biohazardous materials are in use.

Prior to initiating any work on this approved project, please contact me by email (luongo@oakland.edu) to schedule a startup Biosafety Audit. This audit will verify that all biosafety controls described in your application have been implemented.

Please let me know if you have any questions. Thank you.

Sincerely,

Domenic Luongo, CHMM
Director - Laboratory Safety and Compliance

(email ID #400090)

*** THIS IS AN EMAIL NOTIFICATION ONLY. PLEASE DO NOT REPLY ***

From: eSirius3GWebServer no-reply@esirius.cayuse.com
Subject: Committee Action Record – New or De Novo IACUC Protocol # 2021-1131 Approval
Date: January 9, 2025 at 9:57 AM
To: tonyushkin@oakland.edu

E



Reference: IACUC Protocol # 2021-1131

Protocol Title: A Single-Sided Magnetic Particle Imaging Scanner for In Vivo Breast Cancer Imaging

Principal Investigator: Tonyushkin, Alexey

Approval Period: 01/09/2025 - 01/09/2028

Dear Professor Tonyushkin, Alexey:

The Institutional Animal Care and Use Committee (IACUC) has reviewed the original proposal, noted the required modifications provided by you upon committee's request (if applicable), and approved the project referenced above.

The proposed activities are approved for a period of three years, starting 01/09/2025 and ending 01/09/2028, and assigned the approval # IACUC-2021-1131. This is your formal approval notice; please save it for your records. Be aware that protocols expire at 12:01 AM on the expiration date. Ninety (90) days before the protocol approval expires, Cayuse will send you an alert email prompting you to submit a De Novo application to renew the project, if desired.

Any unanticipated problems, changes in, or halting of the activities proposed in the project, as described, must be promptly reported to the IACUC Administrator.

In addition, all faculty, staff, and students involved in the project must be trained and qualified to conduct the project in a responsible manner. Please note, in this regard, that you, the Principal Investigator, are fully responsible at all times.

Please let me know if you have any questions.

Sincerely,

Rick Marble
Animal Research Facility Manager and IACUC Administrator

(email ID #400004)

*** THIS IS AN EMAIL NOTIFICATION ONLY. PLEASE DO NOT REPLY ***

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