Topics in Sparse Inverse Problems and Electron Paramagnetic Resonance Imaging

DISSERTATION

Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

By

Subhojit Som, M. S.

Graduate Program in Electrical and Computer Engineering

The Ohio State University

2010

Dissertation Committee:
Prof. Lee C. Potter, Adviser
Prof. Philip Schniter
Prof. Randolph L. Moses
ABSTRACT

In this thesis we address two inverse problems. The first is the reconstruction of sparse signals. In the second, electron paramagnetic resonance imaging (EPRI) is considered.

The problem of recovering sparse signals has recently generated much interest among researchers. The research in this area has led to development of faster algorithms with provable performance guarantees. The sparse algorithms can significantly reduce the amount of data required for extracting information of interest from observations. In this thesis we consider the sparsity pattern recovery problem under a probabilistic signal model where the sparse support follows a Bernoulli distribution and the signal restricted to this support follows a Gaussian distribution. For the maximum aposteriori estimate, we show that the energy in the original signal restricted to the missed support is bounded above; the bound is of the order of the energy in the noise signal projected to the subspace spanned by the active coefficients of the original signal. We also derive sufficient conditions for no missed detection and no false alarm in support recovery.

Electron Paramagnetic Resonance Imaging (EPRI) is an imaging modality which has a great potential for clinical oximetry applications for cancer treatment and wound healing. Because of several reasons including long data collection time and low signal-to-noise ratio (SNR), this modality has not yet become a clinically successful method.
We address these two problems in this thesis. We use the structure present in the EPR spectrum in the form of both Lorentzian line shape and sparse nature of the spin probes implanted for oximetry. We experimentally demonstrate that this leads to two orders of magnitude reduction in data acquisition time. We also propose and build a digital data acquisition system that enhances SNR by enabling simultaneous acquisition of multiple harmonics of both absorption and dispersion components of the signal. A novel convergent iterative algorithm is proposed for processing the data in the presence of phase noise and unknown microwave phase.
to my parents
ACKNOWLEDGMENTS

I would like to thank my advisor, Prof. Lee Potter, for his guidance and help during the course of this research work. It has been a nice experience working with him, both academically and personally. I would also like thank Prof. Philip Schniter for his guidance during the work on support recovery. I thank Prof. Randolph Moses for his guidance during my early days at Ohio State. I thank all of them and Prof. Bruce Weide for agreeing to be on my exam committee.

Part of the work presented in this thesis was done jointly with Rizwan Ahmad. He has been a very helpful friend and guide in my endeavor to work with EPR imaging. I am grateful to Prof. Kuppusamy and Prof. Zweier for allowing me to use their laboratory.

I have always enjoyed the company of my IPS labmates. Thanks to all of them for making this place wonderful. Jeri has always been full of energy in her efforts in making IPS a better place.

All my former roommates during these years – Soumya, Sugumar, Anand and Amit have made my life at Columbus really enjoyable. I thank all of them for being such nice friends. I thank Sanjoy, Tathagata, Sukirti, Petru, Hernan, Lifeng, Arun, Praveen, Sib, Rahul, Justin, Aniruddha, Pritam, Abon, Prateeti, Debraj, JB, Taniya, Anurupa, Aritra, Indrajit, Sujoy for the great time I have spent at Columbus.
I would specially thank Debasish who has been a great friend. I have been fortunate to have his friendship.

I am thankful to my parents Subrata and Subhra Som for their love, support, and all the things they have done for me. They have done extremely hardwork to ensure that my brother and I get good education in spite of being brought up in a rural area. I thank my brother Supratik for his love and all the good times we have spent together. I thank dida and Munu masi for their encouragement.

Finally, I express my gratitude to my wife Amrita for her love, support and sharing the ups and downs in life with a smiling face. I am lucky to have her in my life.
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CHAPTER 1

INTRODUCTION

The focus of this thesis can be broadly divided into two parts. The first deals with recovery of sparse signals, whereas the second deals with Electron Paramagnetic Resonance Imaging (EPRI). The objective of this introductory chapter is to give a background on the topics, describe the major contributions made, and provide an outline of the remaining chapters.

In sparse signal recovery, the problem of estimating a sparse signal is considered. By sparse signal we mean a vector with few nonzero entries. Extensive research work in the recent past [1,2,3,4,5] in this area has shown that sparse signals can be robustly recovered from a small number of observations. In many applications it is not only necessary to estimate the sparse signal, but also important to know the posterior distribution of the signal. We consider a Bayesian framework to address this aspect and present some results on the support set estimation of probabilistically modeled sparse signals.

EPRI is an imaging modality which has a great potential for clinical oximetry applications for cancer treatment and wound healing [6,7,8,9]. But in spite of this great potential it is not yet a clinically successful method due to three main reasons: long data collection time, low signal-to-noise ratio (SNR) and lack of clinically safe
and sensitive probe materials. While there has been a significant amount of work done on the probe development aspect in the recent years [10, 11, 12, 13, 14, 15, 16], this topic is beyond the scope of our work. We address the issues of prohibitively long data acquisition time and low SNR. We propose a parametric imaging model for EPRI which enables proper exploitation of the structure present in the EPR spectra. We also propose an algorithm to exploit the sparse structure in the implanted probes, motivated by recent research in sparse signal recovery. These two ideas have led to approximately two orders of magnitude reduction in data acquisition time, turning hours into minutes. In addition, we have proposed a new EPR signal receiver architecture and the associated signal processing techniques. Previous EPR signal receivers were capable of collecting only the first harmonic absorption signal. We propose, build, and demonstrate a new digital receiver architecture to enhance the effective SNR by capturing multiple harmonics of both the absorption and dispersion components of the EPR spectra by digital subsampling.

The next section gives an outline of the remaining chapters and highlights the contributions.

1.1 Thesis Outline and Contributions

In this section an outline of the thesis is given. Scientific contributions are mentioned and references to the published materials are provided.

Chapter 2

In Chapter 2 a basic overview is given and some relevant background material on sparse reconstruction is presented.
Chapter 3

In Chapter 3, an overview of electron paramagnetic resonance imaging is given. A few EPR imaging techniques are discussed and a brief overview of existing data acquisition techniques is provided.

Chapter 4

In Chapter 4, the problem of support recovery or sparsity pattern recovery is considered where the aim is to identify the non-zero elements of the sparse vector from noisy linear observations. A Bernoulli-Gaussian signal model for the sparse vector is adopted where sparse support is modeled as Bernoulli distributed, and given this support, the signal vector is modeled as Gaussian distributed. Properties of the maximum a posteriori (MAP) estimate of the support set is analyzed and finite sample bounds on partial support recovery are obtained. It is shown that the energy in the original signal restricted to the missed support of the MAP estimate is bounded above and this bound is of the order of energy in the projection of the noise signal to the subspace spanned by the active coefficients. A sufficient condition for perfect support recovery under this signal model is also derived. The material of this chapter is based on:

S. Som, and L.C. Potter,

“Sparsity Pattern Recovery in Bernoulli-Gaussian Signal Model”
Chapter 5

In Chapter 5 a parametric model for spectral-spatial imaging is proposed and demonstrated experimentally with a one-dimensional spatial object. This model assumes Lorentzian lineshape for the EPR spectrum, but any other parametric form can be adopted. This new approach reduces the effective dimensionality of the image reconstruction problem. For example, for a 2D spectral-spatial image reconstruction with grid size $N^2$, the dimensionality reduces to $2N$. Cramér-Rao bound analysis is presented, and simulation results show that the maximum likelihood estimator achieves this bound. The material of this chapter is based on:

S. Som, L.C. Potter, R. Ahmad, and P. Kuppusamy,
“A Parametric Approach to Spectral-spatial EPR Imaging”

Summary of the results has also been published as:

S. Som, L.C. Potter, R. Ahmad, and P. Kuppusamy,
“Reduced Acquisition EPR Oximetry”
A Joint Conference of 12th In Vivo EPR Spectroscopy and Imaging, and 9th International EPR Spin Trapping/Spin Labeling, Chicago, IL, 2007.

Chapter 6

In Chapter 6 the sparse nature of the multi-site EPR oximetry is exploited. A two step algorithm is proposed. In the first step, using a linearized forward model, approximate locations of the implants are determined. In the second step, the true nonlinear forward model is used to estimate the spin density and linewidth but only
for the voxels around the identified approximate implant locations. Non-ideal system behaviors like magnetic field drift are also modeled, and the corresponding parameters are estimated. It is experimentally demonstrated that adoption of a parametric model and use of the sparse structure enables about two orders of magnitude reduction in data collection time. The material of this chapter is based on:

S. Som, L.C. Potter, R. Ahmad, D.S. Vikram, and P. Kuppusamy,

“EPR Oximetry in Three Dimensions using Sparse Spin Distribution”

Summary of the results has also been published as:

S. Som, L.C Potter, R. Ahmad, D.S. Vikram, and P. Kuppusamy,

“Rapid EPR Oximetry Using Sparse Spin Distribution”

Chapter 7

In Chapter 7 a new quadrature digital receiver and associated signal estimation procedure are reported for L-band EPR spectroscopy. The approach provides simultaneous acquisition and joint processing of multiple harmonics in both in-phase and out-of-phase channels. The digital receiver, based on a high-speed dual channel analog-to-digital converter, allows direct digital down conversion with heterodyne processing using digital capture of the microwave reference signal. Thus, the receiver avoids noise and nonlinearity associated with analog mixers. Also, the architecture allows for low-Q anti-alias filtering and does not require the sampling frequency to be time-locked to the microwave reference. A noise model applicable for arbitrary
contributions of oscillator phase noise is given, and a corresponding maximum likelihood estimator of unknown parameters is also reported. The estimation is carried out using a convergent iterative algorithm capable of jointly processing the in-phase and out-of-phase data in the presence of phase noise and unknown microwave phase. Cramér-Rao bound analysis and simulation results demonstrate a significant reduction in linewidth estimation error using quadrature detection, for both low and high values of phase noise. EPR spectroscopic data are also reported for illustration. The material of this chapter is based on the submission:


Summary of the results has also been published as:


Chapter 8

In Chapter 8 we conclude with some potential research directions most relevant to this work.
Sparsity is inherent in many physical systems and phenomena. If this sparse structure is properly exploited, many computational tasks become manageable which are otherwise intractable with the existing computational resources. Also, many inference problems can be robustly solved from a significantly less amount of data by harnessing sparseness in an appropriate manner. In recent years a significant amount of research has been pursued in the understanding of sparse systems. Better understanding of these systems has led to development of faster algorithms with better performance guarantees. In signal processing and many statistical inference problems from diverse fields of application like medical imaging, astronomy, geophysics, computer vision, bioinformatics, neuroscience, distributed sensor network etc., sparse structures are inherent and there has been a significant impact of sparsity inspired algorithms in these fields. For example, sparse structure is explicit in astronomy problems whereas it is implicit in imaging problems. Since images are compressible, they have sparse representation. In network and graph problems typically a single node is connected to only a few other nodes. Hence these structures are sparse. In many statistical inference problems the high dimensional data lie on a low dimensional manifold whose dimension is significantly smaller than the ambient dimension. This is another type
of sparsity. In this digital era when we deal with data of unforeseen size (e.g., digital data acquired from high speed analog to digital converters or internet data) or data with very high dimension (e.g., high resolution radar or medical images, high definition videos), it is important that we study and exploit sparse structure with due diligence.

2.1 Underdetermined Linear System

In sparse reconstruction, a component of compressive sensing, an underdetermined linear system of equations is considered where signals can be recovered from a very small number of observations. The linear observation model is

\[ y = Ax + e, \]  

where \( x \in \mathbb{R}^N \) is the signal vector, \( e \in \mathbb{R}^M \) is the noise vector, \( A \in \mathbb{R}^{M \times N} \) is the measurement matrix, and \( M \ll N \). In spite of this being an ill-posed problem, various algorithms have been proposed for estimating the unknown signal \( x \) and performance guarantees have been proven for them subject to sparsity of the signal \( x \) and some coherence constraints on the measurement matrix \( A \). If \( K \) denotes the number of non-zero elements in \( x \), \( M = \mathcal{O}(K \log(N/K)) \) observations are sufficient for stable recovery of the sparse signal \( x \) [17].

Algorithms for estimating sparse signals have existed in the literature for several decades [18, 19, 20, 21, 22, 23] but the renewed interest in the area can be attributed to the strong theoretical results and performance guarantees for these algorithms established during the last few years.
2.2 Coherence of Measurement Matrix

Several conditions have been proposed which characterize coherence properties of the measurement matrix $A$ and are used for deriving any performance guarantee for compressive sensing algorithms. Measurement matrix with entries drawn from independent and identically distributed (i.i.d.) Gaussian or Bernoulli distributions, and partial Fourier matrix are known to satisfy these properties. In [3], it is shown that if the mutual coherence \( i.e., \) the magnitude of the maximum entry of the Gram matrix \( m(A) = \max_{i,j:i \neq j} |(A^T A)_{i,j}| \) is small, stable recovery occurs when the number of non-zeros is at most \((m^{-1} + 1)/4\). Another condition, known as restricted isometry property (RIP), is proposed in [4]. The measurement matrix $A$ satisfies RIP with \((n, \varepsilon)\), if for every sparse vector $x$ with cardinality of support set $\leq n$,

\[
(1 - \varepsilon)\|x\|_2^2 \leq \|Ax\|_2^2 \leq (1 + \varepsilon)\|x\|_2^2.
\]  

(2.2)

Though determination of RIP of a given matrix is a NP-hard problem, it can be shown [21] that random matrices satisfy RIP with overwhelming probability. In contrast mutual coherence is a verifiable condition but it gives much weaker performance guarantee than RIP.

If $x_1$ and $x_2$ are two $n$-sparse vectors and $A$ satisfies RIP with \((2n, \varepsilon)\) then,

\[
(1 - \varepsilon)\|x_1 - x_2\|_2^2 \leq \|A(x_1 - x_2)\|_2^2 \leq (1 + \varepsilon)\|x_1 - x_2\|_2^2.
\]  

(2.3)

Thus if $\varepsilon$ is small, then $A$ nearly preserves the distance between any two $n$-sparse signals. Hence if it is known apriori that the unknown signal $x$ is $n$-sparse then it can be recovered from the linear transformation $Ax$ in the presence of a small amount of noise.
2.3 Sparse Reconstruction Algorithms

Three major classes of algorithms have been proposed for sparse reconstruction problems: convex optimization, greedy search and iterative thresholding. The convex ℓ₁-optimization algorithms are of the first category. If the noise norm is bounded by γ, i.e., ∥e∥₂ ≤ γ, then

\[
\hat{x} = \arg \min_x \|x\|_1 \quad \text{subject to} \quad \|Ax - y\|_2 \leq \gamma
\]  

(2.4)
satisfies ∥\hat{x} - x_0∥₂ ≤ C · γ for sparse signals x [4]. The constant C depends on the RIP of the measurement matrix A. The noiseless formulation of (2.4), i.e., when γ = 0, known as Basis Pursuit, was proposed in 1993 [21]. The success of this then ad hoc algorithm eventually led to the emergence of the field of compressive sensing.

The dual of the convex optimization (2.4) is

\[
\hat{x} = \arg \min_x \frac{1}{2}\|Ax - y\|_2 + \lambda \|x\|_1.
\]  

(2.5)
The solution of this optimization also gives stable and reliable sparse solution. The dual of the optimization (2.5), known as LASSO [25] also gives sparse solution, and its properties are well studied:

\[
\hat{x} = \arg \min_x \|Ax - y\|_2 \quad \text{subject to} \quad \|x\|_1 \leq \tilde{\gamma}.
\]  

(2.6)

A non-convex variant of the convex optimization (2.4), given by

\[
\hat{x} = \arg \min_x \|x\|_p \quad \text{subject to} \quad \|Ax - y\|_2 \leq \gamma,
\]  

(2.7)
where p < 1, also guarantees stable recovery of sparse signals [26]. Although it is not always possible to achieve a global minimum of (2.7), extensive numerical simulations suggest that the local minima also give sparse solution with low reconstruction error [26].
Several greedy algorithms have been proposed for sparse signal recovery from undersampled data. These algorithms are motivated by Matching Pursuit (MP) and its modification Orthogonal Matching Pursuit (OMP) algorithms. OMP identifies one active element in the unknown vector at a time in a greedy way, i.e., it selects the column which is most correlated with the residual where residual is the component of the data vector in the orthogonal complement of the subspace spanned by the already selected columns. It has been shown that OMP can recover a sparse signal accurately in the noiseless Gaussian measurement system (i.e., the entries of the measurement matrix are drawn from i.i.d. Gaussian distribution) with a very high probability. But there is no performance guarantee for OMP with noisy data. Several modifications of OMP like Stagewise Orthogonal Matching Pursuit (StOMP), Regularized Orthogonal Matching Pursuit (ROMP), Compressive Sampling Matching Pursuit (CoSaMP), and Subspace Pursuit (SP) have been proposed which identify multiple coefficients at a time at every stage but also eliminate some of them at a later stage, if needed. In case of ROMP, CoSaMP and SP, upper bounds on estimation error have been established.

The third category consists of iterative thresholding algorithms. These algorithms iterate between the following two steps:

\[ x^{t+1} = \eta(x^t + \kappa A^T r^t; \tau) \]  
\[ r^t = y - Ax^t. \]  

Here \( x^t \) is the estimate of the signal and \( r^t \) is the residual at the \( t^{th} \) iteration. \( \kappa \) is a relaxation parameter. The function \( \eta(\cdot) \) is a component-wise scalar nonlinear threshold function which depends on the threshold parameter \( \tau \). Two major classes of thresholding operations and their variants are proposed for sparse signal recovery.
Fig. 2.1: Soft thresholding function \( \eta(x; \tau) = \text{sign}(x)(|x| - \tau)_+ \) with threshold parameter \( \tau = 2 \).

Soft thresholding function is given by

\[
\eta(x; \tau) = \text{sign}(x)(|x| - \tau)_+, \tag{2.10}
\]

where \((y)_+ = 0\) if \(y \leq 0\) and \((y)_+ = y\) if \(y > 0\). Fig. 2.1 shows the soft threshold function for threshold parameter \(\tau = 2\). The hard thresholding function is given by

\[
\eta(x; \tau) = x \times 1_{\{|x| - \tau \geq 0\}}, \tag{2.11}
\]

where \(1_{\{b \geq 0\}}\) is an indicator variable, i.e., if \(b \geq 0\), then \(1_{\{b \geq 0\}} = 1\), and \(1_{\{b \geq 0\}} = 0\), otherwise. Fig. 2.2 shows the hard threshold function for threshold parameter \(\tau = 2\).

In chapter 6, we will use the convex \(\ell_1\)-optimization technique for detecting sparse EPR implants.
$y = \eta(x; \tau) = x \times 1_{(|x| - \tau \geq 0)}$ with threshold parameter $\tau = 2$.

2.4 Probabilistic Sparse Signal Model

In chapter 4 we take a Bayesian approach to the inference of sparse signals. In particular, we model the support of the sparse signal using the hidden binary indicators $\{s_n\}_{n=1}^N$, where $s_n \in \{0, 1\}$. Here, $s_n = 1$ indicates $x_n \neq 0$ w.p. 1 while $s_n = 0$ indicates $x_n = 0$ w.p. 1. The binary vector $s = [s_1, s_2, \ldots, s_N]^T \in \{0, 1\}^N$ describes the signal support. Conditioned on $s$, we assume that the coefficients are independent and follow a spike and slab prior \cite{40} of the form

$$p_n(x_n | s_n) = s_n q_n(x_n) + (1 - s_n)\delta(x_n), \quad (2.12)$$

where $\delta(.)$ denotes the Dirac delta and $q_n(.)$ is a pdf with positive variance and zero mass at origin.
In chapter 4 we derive results about bounds on support detection by constrained MAP estimation of $s$. The next section outlines some prior work on support detection or sparsity pattern recovery.

### 2.5 Sparsity Pattern Recovery

Sparsity pattern recovery is the problem of identifying the non-zero elements of the sparse signal, i.e., estimating the hidden indicator variables $s_n$. A significant amount of work has recently appeared for signal recovery in the context of compressive sensing. The $\ell_2$-norm of error in estimating the signal $x$ is the most popular performance metric \[4, 3, 33\], but in the noisy setting, stability of the solution and boundedness of this performance metric do not give any direct guarantee about support recovery. There are several aspects of sparsity pattern recovery which have been studied earlier. Here we discuss some of the results which are most relevant to our work. In \[41, 42, 43, 44, 45, 46\], the minimum number of observations $M$ needed for partial or perfect support recovery is investigated for deterministic signals. Necessary and sufficient conditions for exhaustive search based decoders and $\ell_1$-constrained least squares are derived in these articles. These results are asymptotic and they consider different sparsity regimes, e.g., linear (where $K/N \to \alpha$, for fixed fraction $\alpha$) and sublinear (where $K/N \to 0$ as $N \to \infty$) regimes, and study the relationship between $N, K$ and $M$ for support recovery guarantees.

Results have been reported on support detection under a probabilistic signal model but they are also asymptotic in nature. For example, using a replica method, Guo et
al. showed \cite{47} that the posterior distribution of a single coefficient becomes asymptotically decoupled from the other coefficients. Detecting a single coefficient is analogous to detecting this input coefficient with all other coefficients suppressed, but based on a noisier observation. They derived the maximum probability of making an error in detecting a single coefficient and the corresponding minimum mean squared error (MMSE) under the high SNR and large system limits. Rangan et al. \cite{48} use the same replica method to obtain the mean squared error in estimation of the variable $\mathbf{x}$ under the large system limits for linear, LASSO, and zero-norm regularized estimators.

For fixed signal dimension, performance of the $\ell_1$-constrained least squares estimator has been studied. Donoho et al. \cite{3} showed that the $\ell_1$-constrained quadratic program with exaggerated noise level guarantees partial support recovery. They also derived an upper bound on the number of non-zero elements in the signal vector for perfect support recovery using an orthogonal greedy algorithm; the bound is given in terms of mutual coherence of the measurement matrix and minimum absolute value of the non-zero elements in the true signal. Candès et al. showed \cite{49} that if the measurement matrix satisfies certain coherence properties and the signs of the non-zero elements of the signal are equally likely to be positive and negative, then $\ell_1$-regularized least squares solution recovers the signed support perfectly with very high probability when the regularization constant is chosen appropriately and the minimum absolute value of the non-zero elements of the signal is above a certain threshold. Recovery of signed support means the support sets of the true signal and the estimate are identical and the non-zero elements in the true signal and the estimate have the same signs. Zhao et al. showed \cite{50} that the irrepresentable condition
is sufficient for LASSO to select the true model both in the fixed $N$ setting and in the large $N$ setting as the observation size $M$ gets large. In special scenarios this irrepresentable condition coincides with the coherence condition used in the work of Donoho et al. [3]. A similar condition is used by Meinshausen et al. [51] to prove a model selection consistency result for Gaussian graphical model selection using the LASSO.
CHAPTER 3

ELECTRON PARAMAGNETIC RESONANCE IMAGING

Electron paramagnetic resonance (EPR) is a phenomenon in which radio frequency (RF) energy is absorbed by unpaired electrons in a magnetic field. In EPR imaging this absorption is measured, and tomographic techniques are used to reconstruct the unpaired electron spin density distribution in space. Presence of oxygen or other paramagnetic materials alters the nature of the absorption spectra, and techniques have been devised to use this property of EPRI to measure oxygen distribution in space. One such technique is Spectral-Spatial EPR Imaging. We use this modality for oximetry applications.

EPR oximetry is proposed for mapping oxygen partial pressure (pO$_2$) at tumor or wound locations. Knowledge of oxygen partial pressure is important for the diagnosis and treatment of cancer and for wound healing. Unlike EPR oximetry, existing technologies are mostly invasive and cannot provide repetitive oxygen measurement precisely at the very same location over a long period of time. Thus monitoring response to treatment is difficult with them. In EPR oximetry, sparse spin probes are implanted in the region of interest. So the technique is invasive, but this has to be done only once. Then reliable oxygen measurement from the sites of these probes can be obtained in a non-invasive way for a long period of time (up to a few years).
In the following sections, we briefly introduce several concepts for EPR: spectral-spatial imaging, oximetry, existing receiver architecture, and existing image reconstruction techniques.

3.1 EPR Spectrum

In EPR, radio frequency (RF) energy is absorbed by unpaired electrons in a magnetic field. When the magnetic field is slowly varied the amount of energy absorbed changes. This absorption plotted against the external magnetic field gives the spectrum. The spectral lineshapes of EPR often have nice parametric forms, and in many cases a lineshape can be approximately represented by a Lorentzian function \[56\].

The Lorentzian function \( L(h) \), as a function of magnetic field \( h \), is given by,

\[
L(h) = \frac{1}{\pi \left( h - h_0 \right)^2 + \left( \frac{\tau'}{2} \right)^2}
\]  \hspace{1cm} (3.1)

where \( h_0 \) is the location of the peak of the lineshape and \( \tau' \) is the linewidth. Linewidth is defined as the width of the region where the function has a magnitude of more than half of its maximum as shown in Fig. 3.1. The area under the Lorentzian curve is constant, i.e.,

\[
\int_{-\infty}^{+\infty} L(h) dh = 1
\]  \hspace{1cm} (3.2)

For notational simplicity half-linewidth \( \tau = \frac{\tau'}{2} \) will be used instead of linewidth \( \tau' \) and the constant factor of \( \frac{1}{\pi} \) will be omitted throughout this thesis.

3.2 Physics Behind Lineshape

The analytical derivation of lineshape from first principle physics is nicely described in \[57\]. In the presence of an external magnetic field the electron spin states

\(^1\)Some of the sections are adapted from our previous work in \[52, 53, 54, 55\].
Fig. 3.1: Lorentzian function with $\tau' = 1.0$ and $h_0 = 0$. 
and energies are quantized to distinct levels. This is known as the Zeeman Effect. Another time-varying external magnetic field causes state transitions. The energy absorbed during these transitions is measured in EPR. The interaction between electron spins, the main static magnetic field $B_0 = B_0 \hat{z}$ and the orthogonal time-varying magnetic field $B_1$ can be given by Bloch equations. It can be shown\textsuperscript{[57]} that the intrinsic dispersion and absorption lineshape as a function of magnetic field $B$ are given by,

$$M_x'(B) = \frac{\gamma^2 B_1 T_2^2 (B_0 - B)}{1 + \gamma^2 T_2^2 (B_0 - B)^2 + \gamma^2 B_1^2 T_1 T_2} M_0$$

$$M_y'(B) = \frac{\gamma^2 B_1 T_2}{1 + \gamma^2 T_2^2 (B_0 - B)^2 + \gamma^2 B_1^2 T_1 T_2} M_0$$

where $\gamma$ is the gyromagnetic ratio of the electron, $M_0$ the net magnetization due to $B_0$ prior to perturbation by $B_1$, $T_1$ the longitudinal relaxation time and $T_2$ the transverse relaxation time.

Eqn. (3.4) shows why the lineshape is well approximated as a Lorentzian. If $\gamma^2 B_1^2 T_1 T_2 \ll 1$, eqn. (3.4) becomes a Lorentzian with half-linewidth of $\frac{1}{|\gamma T_2|}$. This is independent of $T_1$. But as $\gamma^2 B_1^2 T_1 T_2$ increases the Lorentzian starts saturating and the half-linewidth becomes dependent on $T_1$.

In some practical cases the lineshape is much more complicated due to the effects of neighboring unpaired nuclear spins in the free radical molecule. These magnetic fields cause further splits of the electron energy states which result in the hyperfine splitting. Instead of a single peak, multiple peaks are present.

### 3.3 Line Broadening

Unlike Magnetic Resonance Imaging (MRI) where nuclear spin from the animal body can be used to capture an image, injection of external spin probes is needed for
EPR imaging. In EPR oximetry, these spin probes interact with oxygen present in the body to cause EPR phenomena.

In the presence of oxygen or other paramagnetic materials the unpaired electrons interact with the spin probe to yield a Heisenberg spin exchange. This causes line broadening. The amount of broadening is proportional to the frequency of collision between the spin probe and oxygen \[57\]. The frequency of collision is given by the Smoluchowski equation,

\[ \omega_{O_2} = 4\pi \delta_{\text{mol}} (D_{O_2} + D_P) \rho_{O_2} \]  

where \( \delta_{\text{mol}} \) is the distance between centers of the colliding paramagnetic molecules, \( D_{O_2} \) and \( D_P \) are the diffusion coefficients of oxygen and spin probe and \( \rho_{O_2} \) is the concentration of oxygen molecules. In most practical scenarios \( D_{O_2} \) is much greater than \( D_P \). In vivo the \( D_{O_2} \) approximately equals the diffusion coefficient of water \( D_{H_2O} \). The change in intrinsic linewidth can be given by,

\[ \Delta(\tau') \approx \frac{4\pi}{|\gamma|} p_{ex} \delta_{\text{mol}} D_{H_2O} \rho_{O_2} \]  

where \( p_{ex} \) is the probability of an observable event due to spin exchange which is approximately equal to one \[57\]. In eqn. (3.6) all the terms except \( \rho_{O_2} \) are constant and hence the linewidth changes linearly with oxygen concentration.

### 3.4 Spatial EPR Imaging and Deconvolution

In spatial EPR imaging the aim is to determine the spatial distribution of electron spin density. The lineshape function is considered to be constant throughout the object. Under this assumption the measured spectra become a convolution between lineshape function and the projections of spin distribution \[56\]. Projection of an
image is its *Radon Transform* \[58\]. In Fig. 3.2 the Radon Transform is given by,

\[ p(s, \phi) \triangleq Rf = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} f(x, y) \delta(y \sin(\phi) - x \cos(\phi) - s) \, dx \, dy \] (3.7)

Therefore the lineshape function (which is known since the spin probe is known) is typically deconvolved first from the measured projections and then backprojection or Fourier transform based algorithms are applied to obtain the Inverse Radon Transform, *i.e.*, the electron spin density.

### 3.5 Spectral-Spatial Imaging

The deconvolution based technique fails if the lineshape function varies with space. In this scenario the spin density and the lineshape both are typically unknown and need to be estimated \[59\]. Motivated by the Nuclear Magnetic Resonance (NMR)
Fig. 3.3: 1D spatial object. The spin density and linewidth both vary with space.
spectroscopic imaging technique of Lauterbur et al. [60], Maltempo et al. [61] and Ewert et al. [62] independently proposed spectral-spatial EPR imaging to solve this problem. Martin et al. [63, 64] describe the data collection and reconstruction strategies in EPR spectral-spatial imaging.

In spectral-spatial imaging a magnetic field gradient is applied to create a spatially varying magnetic field in such a way that spins at different spatial locations are excited with a different magnetic field; the projection obtained is the Radon Transform of a virtual object with an additional spectral dimension. Any slice of this object along the spectral axis gives the lineshape function at that spatial location amplified by the spin density of the same location.

This concept can be illustrated with the simple 1D spatial object in Fig. 3.3. Spectral-spatial imaging creates projections of a virtual 2D spectral-spatial object with one spatial dimension and one spectral dimension. This is illustrated in Fig. 3.4.

Fig. 3.5 shows the magnetic field generation for 2D spectral-spatial imaging. There are two magnetic fields in this case: one creates a field gradient along the spatial axis and the second one is constant. Let the line DC show the magnetic field generated at different spatial locations due to the gradient and assume that the constant magnetic field is zero. Therefore the energy absorption is the projection of this virtual object along the line DC. Now if the constant magnetic field is increased by $\Delta H$ then the magnetic field generated at various spatial locations is given by the line SR. The energy absorption is thus given by the projection along the SR line. So by sweeping the constant magnetic field, projection samples at angle $\phi$ can be obtained. Then the gradient is changed to obtain projection samples at another angle.
Fig. 3.4: 2D spectral-spatial object generated from the spin and linewidth profile of Fig. 3.3.
Fig. 3.5: Magnetic field generation for 2D spectral-spatial imaging. Sweeping the constant magnetic field creates spatially varying fields represented by parallel lines AB, CD, RS and EF. Changing the gradient field changes the angle $\phi$. 
3.6 Reconstruction in Spectral-Spatial Imaging

3.6.1 Assumptions

For the existing reconstruction techniques it is assumed that the spectral window is broad enough to capture almost the entire area under the Lorentzian curve. In Fig. 3.5 for the projection along the line AB, only contribution from segment AM is considered and the contribution from MB is ignored.

3.6.2 Reconstruction Techniques

The spectral-spatial object is reconstructed from the projections by the Inverse Radon Transform,

$$f(x, y) \triangleq \mathcal{R}^{-1} p = \frac{1}{2\pi^2} \int_0^\pi \int_{-\infty}^\infty \frac{(\partial p/\partial s)(s, \phi)}{y \sin(\phi) - x \cos(\phi) - s} \, ds \, d\phi \quad (3.8)$$

Either the filtered back-projection or the direct Fourier transform based methods can be used to compute the inverse Radon transform [58].

3.6.3 Determination of Spin Density and Linewidth

After the spectral-spatial object is reconstructed the spin density and linewidth can be determined by a curve-fit at each spatial location. The spin density may also be obtained by integrating the object along the spectral axis at each spatial location since by eqn. (3.2) the area under the spectral axis is independent of the linewidth and thus proportional to the spin density.

3.6.4 Limited Angle Tomography

Due to a hardware limitations on the gradient field strength, the projections at very high angles are not measurable. Stillman et al. [65] proposed a technique
where curve-fit and back-projection are done iteratively. After one iteration of back-projection, Lorentzians are fit to the spectral-spatial image and more projections (at missing angles) are synthetically computed and used to augment the set of measured projections. A few iterations improve the reconstructed image quality.

3.7 EPR Oximetry

EPR oximetry, first reported by Hyde [66] and later extensively investigated by Swartz and colleagues [67, 68, 69, 70], enables repeated measurements of oxygen concentrations in living tissues. In vivo oximetry [71, 72, 73, 74] is the measurement of partial pressure of oxygen (pO$_2$) by observing oxygen-induced broadening in the lineshape of an introduced paramagnetic probe. Upon interaction with a spin probe, oxygen increases the relaxation rate of the probe, mainly via Heisenberg exchange. This leads to an oxygen concentration dependent increase in the linewidth of the probe. The changes in linewidth as a function of pO$_2$ are well characterized for a number of EPR probes. Thus, for a known probe, the change in EPR linewidth can be regarded as a direct measure of pO$_2$. The uniqueness of the method is its ability to report the absolute value of pO$_2$.

EPR oximetry requires the incorporation of an oxygen sensitive paramagnetic spin probe, such as a solid particulate, into the tissue of interest. Considerable progress has been made in the development of oximetry probes [75, 76, 77, 78, 79, 80, 81, 82]. Lithium octa-n-butoxy-substituted naphthalocyanine radical (LiNc-BuO) is a recently developed particulate oximetry spin probe [79]. The LiNc-BuO crystals are composed of stacks of neutral radicals of lithiated naphthalocyanine macrocycles. The EPR spectra of these particulates are characterized by a narrow Lorentzian absorption under
anoxic conditions. The biostable particulates are capable of sensing and reporting cellular and tissue pO$_2$ with oxygen sensitivity better than 0.1 mmHg. This enables precise, accurate and repeated measurement and mapping of oxygen in tissues over extended periods of time.

EPR oximetry holds promise for several clinical applications. In tumors, the oxygen concentration is useful in determining the response to different treatment options [83, 84, 85, 86, 87, 88]. Likewise, the presence of oxygen plays a critical role in the pathophysiology of myocardial injury during both ischemia and subsequent reperfusion [89]. Therefore, the ability of EPR oximetry to make repeated minimally invasive measurements of oxygen over time can provide vital information to characterize the progression of a disease state, and to determine the efficacy of different treatment options. Unfortunately, long data acquisition times have curtailed wider use of EPR for these applications.

### 3.8 EPR Oximetry Techniques

*In vivo* 2D spectral-spatial EPR imaging was demonstrated at 250 MHz with curve fitting used as post-processing to estimate spectral parameters [71]. Spectral-spatial EPR was subsequently extended to 4D imaging. Four-dimensional imaging of an isolated rat heart was demonstrated with an L-band system [90]; oxygen concentration was inferred from peak-to-peak linewidths at each spatial location. Elas *et al.* [91] improved SNR using high-magnitude Zeeman modulation and estimated linewidths by fitting a parametric spectral model [92] at each spatial location in a 4D reconstructed image. Continuous-wave (CW) EPR has also been used to measure free induction decay in the single-point (or constant time) imaging technique [93, 94]. CW EPR
techniques allow simultaneous detection of multiple paramagnetic species and apply for arbitrary spin distributions.

The spin echo imaging technique gives $T_2$-based oximetric information, in contrast to the $T_2^*$ oxygen dependence exploited in CW spectral-spatial techniques. EPR spin-echo imaging was developed by Eaton et al. [95, 96] at X-band. Recently, Mailer et al. reported spin-echo imaging at 250 MHz [97], demonstrating advantages relative to FID measurement: improved signal strength, no distortion due to instrumental dead time, and reduced acquisition time.

EPR oximetry has also been developed with variable gradient strength but fixed field direction. Swartz et al. have pioneered an approach coined “multi-site oximetry.” A single favorable gradient direction is assumed for which each of several isolated implants is resolved. The EPR lineshape for the probe material is assumed Lorentzian, with unknown half-width at half maximum (HWHM) $\tau$. A spectrum is recorded for each of two gradient magnitudes, $G_2 > G_1$, and the two spectra are therefore related by convolution with a Lorentzian function having HWHM of $\tau(1/G_1 - 1/G_2)$. The linewidth parameter, $\tau$ is then estimated by nonlinear least-squares curve fit; the curve fit is computed on intervals for which spectral components are non-overlapping. In this manner, the linewidth of each probe site is estimated without reconstruction of the unknown projection of the paramagnetic spin density. The key assumption is that lineshapes are resolved with a single, one-dimensional magnetic field gradient. Thus, this method localizes pO$_2$ measurements in one dimension.

Microwave power saturation provides an alternative to magnetic field strength by encoding spectral information into the variation of EPR image intensity. Introduced by Bacic et al. [98], this oximetry technique is based on $T_1$ relaxation of electron
spin. The approach can acquire spectral-spatial information with only twice the acquisition time of spatial imaging \[99\] but has spatially varying image resolution and requires narrow linewidth probes with relatively lower sensitivity to oxygen concentration \[100\].

3.9 Signal Receiver

For EPR, the data are collected by measuring the absorption of electromagnetic radiation, usually in the microwave range, by paramagnetic materials in the presence of an external magnetic field. For imaging applications, an additional magnetic field, in the form of a linear magnetic field gradient, is applied to provide spatial encoding. Recent efforts to accelerate EPR data collection include both hardware and algorithm developments. For example, overmodulation \[101\], fast scan \[102\], rapid scan \[103\], pulsed EPR \[104, 105\], parametric modeling \[106\], adaptive and uniform data sampling \[107, 108\], and multisite oximetry \[109, 110\] have shown potential to accelerate the acquisition process.

The microwave signal reflected from the sample cavity, also called resonator, experiences changes in both amplitude and phase upon magnetic resonance. These changes encode the absorption and dispersion components of the EPR spectra. To avoid \(1/f\) noise, associated with the diode detector commonly employed to demodulate the EPR signal to baseband, it is a common practice to apply field modulation. The process of EPR signal extraction then reduces to diode detection followed by phase sensitive detection (PSD) \[111\]. In the presence of automatic frequency control
(AFC), which locks the source frequency $\omega_c$ to the resonance frequency $\omega_0$ of the sample cavity, only the first harmonic absorption is observed. Other AFC configurations allow capture of the first harmonic dispersion instead [112].

Homodyne detection, involving magnetic field modulation and PSD, remains the most prevalent configuration for CW EPR spectrometers. One obvious limitation of homodyne detection is its inability to collect both absorption and dispersion and to collect multiple field modulation harmonics simultaneously. For cases where the field modulation amplitude approaches or exceeds the intrinsic linewidth of the paramagnetic material, a significant fraction of energy resides in higher harmonics. Therefore, quadrature detection across multiple harmonics can reduce the data collection time, or, equivalently, can improve the signal-to-noise ratio (SNR).

Hyde et al. [113] were the first to demonstrate a technique, using digital heterodyne reception, to simultaneously collect absorption and dispersion spectra across multiple harmonics. Several prototypes were presented [114] to implement the digital receiver. The basic configuration included: (i) downconversion of the microwave signal (reflected from the sample cavity) to an intermediate frequency (IF), (ii) time-locked subsampling of the IF signal without inducing aliasing, and (iii) digital matched filtering.

In 2008, Yen, in his master’s thesis [115], reported linewidth estimation error analysis for jointly processing multiple quadrature harmonics of a Lorentzian lineshape. More recently, Tseitlin et al. [116, 117] reported implementation of a digital heterodyne receiver to collect multiple harmonics of absorption and used nonlinear curve fitting to estimate linewidth information.
CHAPTER 4

SPARSITY PATTERN RECOVERY IN
BERNOULLI-GAUSSIAN SIGNAL MODEL

4.1 Introduction

We consider the linear observation model

\[ y = Ax + e, \]  
   \hspace{1cm} (4.1)

where \( x \in \mathbb{R}^N \) is the signal vector, \( e \in \mathbb{R}^M \) is the noise vector, \( A \in \mathbb{R}^{M \times N} \) is the measurement matrix, and \( M \ll N \). In this chapter we consider the problem of sparse support recovery, also known as sparsity pattern recovery, where the aim is to identify the indices of the non-zero elements of \( x \). The main contribution of this chapter is non-asymptotic analysis of support recovery in terms of quality of the recovered support set. We analyze how much energy of the true signal remains in the missed coefficients under Bernoulli-Gaussian signal prior assumption. Our results are non-asymptotic with fixed model dimensions. As discussed in section 2.5, other support recovery results (except 3 and 49) are asymptotic analyses. Our first result is about partial support recovery. We characterize any support set in terms of the energy in the true signal restricted to this support set. More specifically, we explore
the relationship between energy in the missed support and the noise energy under
the probabilistic model where the signal prior is known. Most earlier partial support
recovery results characterize the fraction of the support recovered \textit{i.e.}, they do not
distinguish between missing the coefficient with the highest absolute value and
the lowest absolute value. To the best of our knowledge the only exception is the
work by Akcakaya \textit{et al.} \cite{45}. They investigated the number of measurements needed
for partial support recovery in terms of fraction of total energy in the true signal
restricted to the recovered support. But their analysis is asymptotic whereas we have
considered fixed model dimensions. Our second result is about sufficient conditions for
guaranteeing no missed coefficient and no false detection for this Bernoulli-Gaussian
signal model when the absolute value of any active coefficient is bounded below with
a very high probability.

\section*{4.2 Problem Statement}

\subsection*{4.2.1 Signal Model}

We consider a probabilistic signal model for the sparse signal $x \in \mathbb{R}^N$. Let $S$
be a set whose entries are drawn from the set $I = \{1, 2, \ldots, N\}$ in such a way
that each entry of $I$ is in the set $S$ with probability $p \ll 1$ and their inclusion in
$S$ is independent of each other. Thus the probability that the cardinality of the
support set $S$ equals $K$ is given by $\mathbb{P}[|S| = K] = \binom{N}{K}p^K(1 - p)^{N-K}$. To enforce
sparsity we also assume that $p < \frac{1}{2}$. Each element of $x$ is identically zero if the
corresponding index is not in the set $S$, otherwise the element is Gaussian with mean
$\mu_1$ and non-zero variance $\sigma_1^2$. The mean $\mu_1$ can be zero or non-zero. Elements of $x$
are distributed independently given the support set. If $x_S$ denotes the vector consisting
of the elements of $\mathbf{x}$ whose indices are in the set $S$, then the vector $\mathbf{x}_S$ follows i.i.d. Gaussian distribution \( i.e., \mathbf{x}_S \sim \mathcal{N}(\mu_1 \mathbf{1}_{|S|}, \sigma_1^2 I_{|S|}) \)^2. Thus $S$ is the support set of the signal vector $\mathbf{x}$ with expected cardinality $E[|S|] = N p \ll N$ and $\mathbf{x}$ is sparse with high probability. This Bernoulli-Gaussian model has been quite popular in the literature for a long time \cite{113,114,120} for modeling sparse vectors in diverse application areas and is also becoming increasingly popular in compressive sensing research \cite{121,122,47}.

### 4.2.2 Coherence of Measurement Matrix

We assume that the measurement matrix $\mathbf{A}$ satisfies RIP with $(4Np, \varepsilon)$. We note here that the constant 4 in the definition of RIP of $\mathbf{A}$ is arbitrary and a matter of convenience. In this thesis we also assume that $\varepsilon = \frac{1}{3}$ in order to obtain simple expressions in our results. Leaving $\varepsilon$ as a parameter makes the results difficult to interpret. We could, more generally, choose any other constant instead of 4 in our definition of RIP for the measurement matrix and likewise choose a different upper bound on the $\varepsilon$-value. These choices lead to different values of the constants appearing in our results.

### 4.2.3 Support Recovery

Here, we consider the problem of support recovery \( i.e., \) identifying the indices corresponding to the Gaussian with $\sigma_1^2$ variance. Assuming additive white Gaussian noise with variance $\sigma_2^2$, \( i.e., \mathbf{e} \sim \mathcal{N}(\mathbf{0}, \sigma_2^2 I_M) \),

\[
\mathbf{y}|S \sim \mathcal{N}\left(\mu_1 \mathbf{A}_S \mathbf{1}_{|S|}, \Phi(S)\right), \tag{4.2}
\]

\(^2\)The vector of ones of size $|S| \times 1$ is denoted by $\mathbf{1}_{|S|}$. Similarly the vector of ones of size $|S_1| \times 1$ is denoted by $\mathbf{1}_{|S_1|}$. It is also denoted by $\mathbf{1}_1$ when there is no ambiguity. The notations $\mathbf{1}_{|S_0|1}$ and $\mathbf{1}_{01}$ are used interchangeably. The same applies to the subscripts used for the identity matrix $I$. 

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where $\Phi(S)$ is given by,

$$
\Phi(S) = \sigma^2 A_S A^T_S + \sigma^2_e I_M. \tag{4.3}
$$

The maximum a posteriori (MAP) estimate of the support set is given by,

$$
\hat{S}_{\text{MAP}} = \arg \max_S p(S\mid y) = \arg \max_S p(y\mid S)p(S)
= \arg \max_S \int_x p(y\mid x, S)p(x\mid S)dx \cdot p(S)
= \arg \min_S \frac{1}{2} \ln \det(\Phi(S)) + \frac{1}{2} (y - \mu_1 A_S 1_{|S|})^T \Phi(S)^{-1} (y - \mu_1 A_S 1_{|S|})
+ |S| \ln \frac{1 - p}{p}. \tag{4.4}
$$

We have adopted a probabilistic model for the number of active elements, the signal and the noise. Though the number of non-zero elements in $x$ has mean $Np \ll N$, it can be as large as $N$ with very small but non-zero probability. Similarly signal and noise energy can be arbitrarily large with vanishingly small but non-zero probability. Nevertheless the quantities like cardinality and energy are bounded with overwhelmingly high probability. Keeping this in mind we study the suboptimal estimator which minimizes the MAP cost function subject to the constraint $|S| \leq 2Np$:

$$
\hat{S} = \arg \min_{S:|S| \leq 2Np} \frac{1}{2} \ln \det(\Phi(S)) + \frac{1}{2} (y - \mu_1 A_S 1_{|S|})^T \Phi(S)^{-1} (y - \mu_1 A_S 1_{|S|})
+ |S| \ln \frac{1 - p}{p}. \tag{4.5}
$$

We define the event $E$ to be the cardinality of the true support being less than or equal to $2Np$. As we see later the event $E$ holds with high probability and the estimator defined in (4.5) satisfies certain performance criteria if event $E$ holds. Here we emphasize that instead of $2Np$ we can use $LNp$ for any other $L > 1$ in the definition of the event as $E$. Similarly we can use any other constraint $|S| \leq QNp$ in
the definition of \( \hat{S} \) in (1.3), where \( Q > 1 \). The choice of \( L = Q = 2 \) is arbitrary in both the definition of the event \( E \) and the definition of \( \hat{S} \); but the choices of \( L \) and \( Q \) are related to the constant used in the definition of RIP satisfied by the measurement matrix \( A \). They are chosen in such a way that \( L + Q \leq n \), when \( A \) satisfies RIP with \((nNp, \varepsilon)\). As mentioned earlier we have arbitrarily chosen \( n = 4 \).

4.2.4 Energy in Missed Coefficients

Our first theorem, as stated below, shows that the total energy in the missed coefficients is of the order of the average energy in the projection of noise to the subspace spanned by the active columns of the \( A \) matrix. Here we make no assumption about the mean of the Gaussian distribution \( \mu_1 \).

**Theorem 1** (Energy Bound on Missed Coefficients). For the signal and observation models under consideration, the \( \ell_2 \)-norm of the signal restricted to the index set of missed coefficients by the constrained MAP estimator is upper bounded by

\[
K_1 \sqrt{Np} \sigma_e \text{ with probability exceeding } (1 - e^{-Np(2 \ln 2 - 1)})(1 - 3e^{-Np(\beta - 1 \ln \beta)}),
\]

where \( K_1 = 2 \left( \sqrt{7\beta + C} + \sqrt{\beta} \right) \), \( C = \ln \left( 1 + \frac{4\sigma^2}{3\sigma_e^2} \right) + 2 \ln \frac{1-p}{p} \) and \( \beta > 1 \).

Different values of the parameter \( \beta \) give different values of the constant \( K_1 \) and also the probability with which the energy in the missed coefficients is bounded by \( K_1^2 Np\sigma_e^2 \). Both \( K_1 \) and the minimum probability are increasing function of \( \beta \). This is natural since as we increase the bound, i.e., make it loose, the probability with which it is satisfied also increases. We also see that the constant \( C \) is dependent on \( p \) and the ratio \( \sigma^2 / \sigma_e^2 \). Thus the constant \( K_1 \) increases as the signal model is known to be more sparse. The dependence of \( K_1 \) on \( \sigma^2 / \sigma_e^2 \) is a bit counterintuitive. As we
discuss in section 4.4, this bound becomes loose at high SNR. At very high value of this ratio, there is very high probability of no missed coefficients.

4.2.5 Perfect Support Recovery

It is hard to recover the support set perfectly for the zero-mean signal model since a significant number of coefficients are close to zero. Hence they are almost impossible to detect in the presence of noise. If the signal mean is high enough to ensure that all the coefficients are well above the noise level then all of them are detected with a high probability. But even then ensuring that no false alarm happens is tough. The sufficient condition that we establish is based on a higher value of the mean. The following theorem states these results.

**Theorem 2** (Sufficient Condition for Perfect Support Recovery). For the signal and observation models under consideration, all active coefficients are detected by constrained MAP estimator i.e., there is no missed coefficient with probability exceeding

\[(1 - e^{-Np(2\log 2 - 1)})(1 - 3e^{-Np(\beta - 1 - \ln \beta)} - e^{-\left(\frac{\beta - 1 - \ln \beta}{2}\right)})\] if \(|\mu_1| > K_2\sigma_1 + K_1\sqrt{Np}\sigma_e\) where \(K_2 = \sqrt{\beta}, \text{ and } \beta, \bar{\beta} > 1\). \(K_1\) and \(C\) are as defined in theorem 1. Perfect support recovery happens with the same probability if \(|\mu_1| > K_3\sigma_1 + K_4\sqrt{Np}\sigma_e\), where \(K_3 = \max\{K_2, 6\sqrt{2\beta Np}\}\) and \(K_4 = \max\{K_1, 3\left(\frac{1}{2} + \sqrt{3}\right)\sqrt{2\beta}\}\).

Here the condition \(|\mu_1| > K_2\sigma_1 + K_1\sqrt{Np}\sigma_e\) is sufficient for probabilistic guarantee for no missed detection. This condition implies that if the distribution of \(x_S\) is such that with very high probability absolute values of all the elements are above the noise level in the subspace spanned by the active columns of the measurement matrix then with very high probability there is no active coefficient excluded from \(\hat{S}\). In addition
to this condition, $|\mu_1| > 6\sqrt{2\beta Np}\sigma_1 + 3\left(\frac{1}{2} + \sqrt{3}\right)\sqrt{2\beta \sqrt{Np}}\sigma_e$ guarantees no false alarm.

4.3 Proofs

4.3.1 Some Propositions

Before proceeding further we provide the following propositions. The first proposition is a consequence of RIP. It shows near orthonormality of the columns of $A$ matrix i.e., the column spaces of any two submatrices $A_i$ and $A_j$ of the matrix $A$ are almost orthogonal to each other if $S_i \cap S_j = \emptyset$ and $|S_i| + |S_j| \leq 4Np$.

**Proposition 1.** If $S_i \subset \{1, 2, \ldots, N\}$, $S_j \subset \{1, 2, \ldots, N\}$, $S_i \cap S_j = \emptyset$, $A$ satisfies RIP with $(4Np, \varepsilon)$ and $|S_i| + |S_j| \leq 4Np$, then the vector induced norm $\|A_i^T A_j\|_2 \leq \varepsilon$.

**Proof.** This proof is due to [33]. Let $S = S_i \cup S_j$. Note that $A_i^T A_j$ is a submatrix of $A_i^T A_j - I_{|S|}$. Since the induced norm of a submatrix never exceeds the norm of the matrix,

$$\|A_i^T A_j\|_2 \leq \|A_i^T A_j - I_{|S|}\|_2 \leq \max\{(1 + \varepsilon) - 1, 1 - (1 - \varepsilon)\} = \varepsilon, \quad (4.6)$$

since the singular values of the matrix $A_i^T A_j$ lie between $1 - \varepsilon$ and $1 + \varepsilon$. \qed

**Proposition 2.** Let $A_i = U_i \Sigma_i V_i^T$ be the Singular Value Decomposition (SVD) of $A_i$. Let $\bar{U}_i$ be the submatrix formed by taking the first $|S_i|$ columns of $U_i$ and $\bar{U}_i$ be the submatrix formed by taking the rest $M - |S_i|$ columns of $U_i$. If $x \in \mathbb{R}^{|S_j|}$, then $\|\bar{U}_i^T A_j x\|_2 \leq \frac{1}{\sqrt{1 - \varepsilon}} \|x\|_2$ and $\|U_i^T A_j x\|_2 \geq \sqrt{\frac{1 - \varepsilon}{1 - 2\varepsilon}} \|x\|_2$. Also, if $v \in \mathbb{R}^{|S_j|}$, then $\|U_i^T \bar{U}_j v\|_2 \geq \sqrt{\frac{1 - \varepsilon}{1 - 2\varepsilon}} \|v\|_2$ where $\bar{U}_j$ is defined similar to $\bar{U}_i$.

**Proof.** From proposition[1] $\|A_i^T A_j x\|_2 \leq \varepsilon \|x\|_2$ and $\|A_i^T A_j x\|_2 = \|V_i \Sigma_i U_i^T A_j x\|_2 = \|\Sigma_i U_i^T A_j x\|_2$ where $\Sigma_i$ is the upper left $|S_i| \times |S_i|$ diagonal submatrix of $\Sigma_i$. Thus
Since elements on $\text{diag}(\bar{\Sigma}) \geq \sqrt{1-\varepsilon}$, we conclude that

$$\| \Sigma_i^T \bar{U}_i^T A_j x \|_2 \leq \varepsilon \| x \|_2.$$  

Now $\| A_j x \|_2^2 \geq (1-\varepsilon) \| x \|_2^2$. Thus $\| U_i^T A_j x \|_2 \geq \sqrt{\frac{1-2\varepsilon}{1-\varepsilon}} \| x \|_2$. Now we can rewrite this as $\| U_i^T \bar{U}_j \Sigma_j V_j^T x \|_2 \geq \sqrt{\frac{1-2\varepsilon}{1-\varepsilon}} \| x \|_2$. Taking $v = \Sigma_j V_j^T x$, we see that $\| U_i^T \bar{U}_j v \|_2 \geq \sqrt{\frac{1-2\varepsilon}{1-\varepsilon}} \| x \|_2 \geq \sqrt{\frac{1-2\varepsilon}{1-\varepsilon}} \| v \|_2$. \hfill \Box

**Corollary 2.1.** If $x \in \mathbb{R}^{\|S\|}$, then for the i.i.d. Gaussian signal model, $x^T A_j^T \Phi(S_i)^{-1} A_j x \geq \frac{1-2\varepsilon}{1-\varepsilon} \frac{\| x \|_2^2}{\sigma_2^2}$. Also the singular values of $A_j^T \Phi(S_i)^{-1} A_j$ are greater than or equal to $\frac{1-2\varepsilon}{1-\varepsilon} \frac{1}{\sigma_2}$.  

**Proof.** We note that,

$$\Phi(S_j) = \sigma_1^2 A_j A_j^T + \sigma_2^2 I_M = U_j (\sigma_1^2 \Sigma_j \Sigma_j^T + \sigma_2^2 I_M) U_j^T,$$ \hspace{1cm} (4.7)

hence,

$$\Phi(S_j)^{-1} = U_j (\sigma_1^2 \Sigma_j \Sigma_j^T + \sigma_2^2 I_M)^{-1} U_j^T,$$ \hspace{1cm} (4.8)

and $A_j^T \Phi(S_i)^{-1} A_j$ is a symmetric and positive definite matrix. Thus

$$x^T A_j^T \Phi(S_i)^{-1} A_j x = x^T A_j^T U_i (\sigma_1^2 \Sigma_i \Sigma_i^T + \sigma_2^2 I_M)^{-1} U_i^T A_j x$$ \hspace{1cm} (4.9)

$$= x^T A_j^T \bar{U}_i (\sigma_1^2 \Sigma_i \Sigma_i^T + \sigma_2^2 I_{|S_i|})^{-1} \bar{U}_i^T A_j x + x^T A_j^T U_i (\sigma_2^2 I_M - |S_i|)^{-1} U_i^T A_j x$$

$$\geq x^T A_j^T \bar{U}_i (\sigma_2^2 I_M - |S_i|)^{-1} \bar{U}_i^T A_j x = \frac{1}{\sigma_2^2} \| U_i^T A_j x \|_2^2 \geq \frac{1-2\varepsilon}{1-\varepsilon} \frac{\| x \|_2^2}{\sigma_2^2}. \hspace{1cm} (4.10)$$

The last inequality follows from proposition \[2\]  Since $A_j^T \Phi(S_i)^{-1} A_j$ is symmetric and positive definite, it has SVD $A_j^T \Phi(S_i)^{-1} A_j = U \Sigma U^T$. Let the $k^{th}$ singular value be $\sigma_k$ and the singular vector corresponding to the singular value $\sigma_k$ be $u_k \in \mathbb{R}^{\|S_i\|}$. Then

$$u_k^T A_j^T \Phi(S_i)^{-1} A_j u_k = u_k^T U \Sigma U^T u_k = \sigma_k.$$ \hspace{1cm} (4.11)

Since $\| u_k \|_2^2 = 1$, from (4.10) and (4.11) it follows that $\sigma_k \geq \frac{1-2\varepsilon}{1-\varepsilon} \frac{1}{\sigma_2}$ and this is true for any $k$. \hfill \Box

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The next proposition is about the tail probability bound of the Chi-squared distribution.

**Proposition 3.** Suppose $n$ independent and identically distributed variables $X_i \sim \mathcal{N}(0, \sigma^2)$. If Chi-squared distributed random variable $Z = \sum_{i=1}^{n} X_i^2$, then for any $\beta > 1$,

$$
P[Z > \beta n\sigma^2] \leq e^{-\frac{n}{2}(\beta - 1 - \ln \beta)}.
$$

(4.12)

**Proof.** Let $\bar{X}_i = \frac{X_i}{\sigma}$. Then $\bar{X}_i \sim \mathcal{N}(0, 1)$ and are independently distributed. Let $\bar{Z} = \sum_{i=1}^{n} \bar{X}_i^2 = \frac{Z}{\sigma^2}$ which is Chi-squared distributed with degree of freedom $n$. Using Chernoff inequality,

$$
P[Z > \beta n\sigma^2] = P[e^{t\bar{Z}} > e^{n\beta t}], \quad \text{for any} \ t > 0
$$

(4.13)

$$
\leq \frac{E[e^{t\bar{Z}}]}{e^{n\beta t}} = \prod_{i=1}^{n} \frac{E[e^{t\bar{X}_i^2}]}{e^{n\beta t}} = \frac{(1 - 2t)^{-\frac{n}{2}}}{e^{n\beta t}}, \quad \text{for} \ t \in (0, 1/2)
$$

(4.14)

The minimum is attained at $t = \frac{\beta - 1}{2\beta}$ which gives inequality (4.12).

We also use the following inequality at various places. If $c, d > 0$, then

$$
\frac{(a + b)^2}{c + d} \leq \frac{(a + b)^2 + (a - b)^2}{c + d} = \frac{2a^2}{c + d} + \frac{2b^2}{c + d} < \frac{2a^2}{c} + \frac{2b^2}{d}.
$$

(4.15)

**4.3.2 Proof of Theorem**

Let us divide the indices for the columns of the $A$ matrix into four disjoint subsets $S_0$, $S_1$, $S_2$ and $S_3$ such that $S_0$ denotes the columns which are in the true support and are correctly identified by the constrained MAP estimator $\hat{S}$, $S_1$ denotes the missed columns, $S_2$ denotes the columns which are not in the true support but selected by
\( \hat{S} \), and \( S_3 \) denotes the columns which are neither in true support nor in \( \hat{S} \). Define \( S_{ij} = S_i \cup S_j \). Let \( A_{ij} \) denote the matrix consisting of those columns of \( A \) which are indexed by the set \( S_{ij} \). Thus,

\[
y = A_{01}x_{01} + e = \mu_1 A_{01}1_{01} + A_{01}z_{01} + e, \tag{4.16}
\]

where \( z_{01} \sim \mathcal{N}(0, \sigma^2_1 1_{|S_{01}|}) \). For zero mean model, \( \mu_1 = 0 \) and \( z_{01} = x_{01} \).

We have defined the event \( E \) to be \( |S_{01}| \leq 2Np \). The mean value of \( |S_{01}| \) is \( \mathbb{E}[|S_{01}|] = Np \). Using Chernoff bound on upper tail of Binomial distribution [123, pp. 68],

\[
\mathbb{P}[|S_{01}| > (1 + \delta)\mathbb{E}[|S_{01}|]] < \left( \frac{e^{\delta}}{(1 + \delta)(1+\delta)} \right)^{\mathbb{E}[|S_{01}|]}. \tag{4.17}
\]

Taking \( \delta = 1 \),

\[
\mathbb{P}[E] = \mathbb{P}[|S_{01}| \leq 2Np] > 1 - e^{-Np(2\ln 2 - 1)}. \tag{4.18}
\]

If \( E^c \) denotes the complement of \( E \) i.e., the event \( |S| > 2Np \), then for any event \( B \),

\[
\mathbb{P}[B] = \mathbb{P}[E]\mathbb{P}[B|E] + \mathbb{P}[E^c]\mathbb{P}[B|E^c] \geq \mathbb{P}[E]\mathbb{P}[B|E]. \tag{4.19}
\]

For the rest of the proof we assume that event \( E \) holds and all the subsequent probabilities are conditioned on event \( E \).

For convenience we define the function to be minimized in (4.5) as \( \gamma(S) \) i.e.,

\[
\gamma(S) = \frac{1}{2} \ln \det(\Phi(S)) + \frac{1}{2}(y - \mu_1 A_S1_{|S|})^T \Phi(S)^{-1}(y - \mu_1 A_S1_{|S|}) + |S| \ln \frac{1 - p}{p}
= \frac{1}{2} \gamma_1(S) + \frac{1}{2} \gamma_2(S) + \gamma_3(S), \tag{4.20}
\]

where \( \gamma_1(S) = \ln \det(\Phi(S)) \), \( \gamma_2(S) = (y - \mu_1 A_S1_{|S|})^T \Phi(S)^{-1}(y - \mu_1 A_S1_{|S|}) \) and \( \gamma_3(S) = |S| \ln \frac{1 - p}{p} \).

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Let the SVD of \( A_0 \) be \( A_0 = U_0 \Sigma_0 V_0^T \). Let \( \bar{U}_0 \) denote the submatrix of \( U_0 \) consisting of the first \(|S_0|\) columns and \( U_0^c \) denote the submatrix with the rest of the columns. Thus \( \bar{U}_0 \) forms an orthonormal basis for the column space \( A_0 \) of \( A_0 \). \( U_0^c \) forms an orthonormal basis for the space \( \mathbb{R}^M \setminus A_0 \). Let \( \Sigma_0 \) denote the \(|S_0| \times |S_0|\) upper left square submatrix of \( \Sigma_0 \). From \( (4.3) \),

\[
\Phi(S_{01}) = \Phi(S_0) + \sigma_1^2 A_1 A_1^T.
\]  

(4.21)

Hence applying matrix determinant lemma,

\[
\gamma_1(S_{01}) = \ln \det(\Phi(S_{01})) = \ln \det(\Phi(S_0)) + \ln \det(I_{|S_1|} + \sigma_1^2 A_1^T \Phi(S_0)^{-1} A_1)
\]

\[
= \ln \det(\Phi(S_0)) + \ln \det(I_{|S_1|} + \sigma_1^2 A_1^T U_0 (\sigma_1^2 \Sigma_0 \Sigma_0^T + \sigma_2^2 I_M)^{-1} U_0^T A_1)
\]

\[
\leq \ln \det(\Phi(S_0)) + |S_1| \ln \left( 1 + \frac{\sigma_1^2}{\sigma_2^2} (1 + \varepsilon) \right). 
\]  

(4.22)

The inequality in \( (4.22) \) follows from the facts that the maximum singular value of the matrix \( A_1 \) is \( \sqrt{1 + \varepsilon} \) and maximum value on the diagonal of the diagonal matrix \((\sigma_1^2 \Sigma_0 \Sigma_0^T + \sigma_2^2 I_M)^{-1} \) is \( \frac{1}{\sigma_2^2} \) and \( \sigma_1^2 A_1^T U_0 (\sigma_1^2 \Sigma_0 \Sigma_0^T + \sigma_2^2 I_M)^{-1} U_0^T A_1 \), being a symmetric and positive definite matrix, has SVD of the form \( U \Sigma U^T \). A lower bound on \( \gamma_1(S_{02}) \) can be obtained proceeding in a similar way as \( (4.22) \) was obtained but taking lower bound instead of upper bound. We note that from corollary \( 2.1 \), the minimum singular value of \( \sigma_1^2 A_1^T \Phi(S_0)^{-1} A_2 \) is at least \( \frac{1 - 2\varepsilon}{1 - \varepsilon} \). Thus

\[
\gamma_1(S_{02}) = \ln \det(\Phi(S_{02})) \geq \ln \det(\Phi(S_0)) + |S_2| \left( 1 + \frac{\sigma_1^2}{\sigma_2^2} \left( 1 - \frac{2\varepsilon}{1 - \varepsilon} \right) \right). 
\]  

(4.23)

Let the SVD of \( A_{01} \) be \( A_{01} = U_{01} \Sigma_{01} V_{01}^T \). Let \( \bar{U}_{01} \) denote the submatrix of \( U_{01} \) consisting of the first \(|S_{01}|\) columns and \( U_{01}^c \) denote the submatrix with the rest of the columns. Thus \( \bar{U}_{01} \) forms an orthonormal basis for the column space \( A_{01} \) of \( A_{01} \).
forms an orthonormal basis for the space \( \mathbb{R}^M \setminus \mathcal{A}_{01} \). The measured data \( \mathbf{y} \) is noisy linear combination of the columns of \( \mathbf{A} \) selected by \( S_{01} \).

\[
\mathbf{y} - \mu_1 \mathbf{A}_{01} \mathbf{1}_{01} = \mathbf{A}_{01} \mathbf{z}_{01} + \mathbf{e} = \mathbf{U}_{01} \mathbf{\Sigma}_{01} \mathbf{V}_{01}^T \mathbf{z}_{01} + \mathbf{e}
\] (4.24)

Let \( \mathbf{e} = \tilde{\mathbf{U}}_{01} \tilde{\mathbf{e}}_{01} + \mathbf{U}_{01} \mathbf{e}_{01} \). Thus from (4.8) and (4.24) and the fact that \( \mathbf{U}_{01}^T \mathbf{A}_{01} \mathbf{z}_{01} = 0 \),

\[
\gamma^2(S_{01}) = (\mathbf{y} - \mu_1 \mathbf{A}_{01} \mathbf{1}_{01})^T \Phi(S_{01})^{-1} (\mathbf{y} - \mu_1 \mathbf{A}_{01} \mathbf{1}_{01})
\] (4.25)

\[
= (\mathbf{U}_{01} \mathbf{\Sigma}_{01} \mathbf{V}_{01}^T \mathbf{z}_{01} + \mathbf{e})^T \mathbf{U}_{01} (\sigma^2 \mathbf{\Sigma}_{01} \mathbf{\Sigma}_{01}^T + \sigma^2 \mathbf{I}_M)^{-1} \mathbf{U}_{01}^T (\mathbf{U}_{01} \mathbf{\Sigma}_{01} \mathbf{V}_{01}^T \mathbf{z}_{01} + \mathbf{e})
\]

\[
= (\mathbf{\Sigma}_{01} \mathbf{V}_{01}^T \mathbf{z}_{01} + \tilde{\mathbf{e}}_{01})^T (\sigma^2 \mathbf{\Sigma}_{01} \mathbf{\Sigma}_{01}^T + \sigma^2 \mathbf{I}_1)^{-1} (\mathbf{\Sigma}_{01} \mathbf{V}_{01}^T \mathbf{z}_{01} + \tilde{\mathbf{e}}_{01}) + \frac{1}{\sigma^2} \| \mathbf{e}_{01} \|_2^2
\]

\[
\leq \frac{(\sqrt{1 + \varepsilon} \| \mathbf{z}_{01} \|_2 + \| \mathbf{e}_{01} \|_2)^2}{(1 - \varepsilon) \sigma_1^2 + \sigma^2} + \frac{\| \mathbf{e}_{01} \|_2^2}{\sigma^2} \quad (4.26)
\]

\[
< \frac{2(1 + \varepsilon) \| \mathbf{z}_{01} \|_2^2}{(1 - \varepsilon) \sigma_1^2} + \frac{2 \| \mathbf{e}_{01} \|_2^2}{\sigma^2} + \frac{\| \mathbf{e}_{01} \|_2^2}{\sigma^2} \quad (4.27)
\]

Now we obtain a lower bound on \( \gamma^2(S_{02}) \). Let the SVD of \( \mathbf{A}_{02} \) be \( \mathbf{A}_{02} = \mathbf{U}_{02} \mathbf{\Sigma}_{02} \mathbf{V}_{02}^T \).

Let \( \tilde{\mathbf{U}}_{02}, \mathbf{U}_{02} \) and \( \mathbf{\Sigma}_{02} \) be defined similar to \( \tilde{\mathbf{U}}_{01}, \mathbf{U}_{01} \) and \( \mathbf{\Sigma}_{01} \) respectively. Let \( \tilde{\mathbf{W}}_{1\setminus02} \) be an orthonormal basis for the subspace spanned by \( \tilde{\mathbf{U}}_{02} \mathbf{U}_{02}^T \tilde{\mathbf{U}}_1 \). Let us denote this subspace by \( \mathcal{A}_{1\setminus02} \). Also, let \( \tilde{\mathbf{U}}_{012} \) be an orthonormal basis for the column space of \( \mathbf{A}_{012} \) and \( \mathbf{U}_{012} \) be an orthonormal basis for the left null space \( \mathbb{R}^M \setminus \mathcal{A}_{012} \). The two subspaces \( \mathcal{A}_{1\setminus02} \) and \( \mathbb{R}^M \setminus \mathcal{A}_{012} \) are orthogonal and their union is the subspace
\[ \mathbb{R}^M \setminus A_{02}. \] Now,

\[
\gamma_2(S_{02}) = (y - \mu_1 A_{02} 1_{02})^T \Phi(S_{02})^{-1}(y - \mu_1 A_{02} 1_{02}) \]  \hspace{1cm} (4.28)

\[
= (y - \mu_1 A_{02} 1_{02})^T U_{02}(\sigma^2_1 \Sigma_{02} \Sigma_{02}^T + \sigma^2_e I_M)^{-1} U^T_{02}(y - \mu_1 A_{02} 1_{02}) \]  \hspace{1cm} (4.29)

\[
= (y - \mu_1 A_{02} 1_{02})^T U_{02}(\sigma^2_1 \Sigma_{02} \Sigma_{02}^T + \sigma^2_e I_{02})^{-1} U^T_{02}(y - \mu_1 A_{02} 1_{02})
+ \frac{1}{\sigma^2_e} ||U^T_{02}(y - \mu_1 A_{02} 1_{02})||^2_2 \]  \hspace{1cm} (4.30)

\[
\geq \frac{1}{\sigma^2_e} ||U^T_{02}(y - \mu_1 A_{02} 1_{02})||^2_2 \]  \hspace{1cm} (4.31)

\[
= \frac{1}{\sigma^2_e} ||U^T_{02}(A_0 x_0 + A_1 x_1 + e - \mu_1 A_{02} 1_{02})||^2_2 \]  \hspace{1cm} (4.32)

\[
= \frac{1}{\sigma^2_e} ||U^T_{02}(A_1 x_1 + e)||^2_2 \]  \hspace{1cm} (4.33)

\[
= \frac{1}{\sigma^2_e} ||W^T_{1,02}(A_1 x_1 + e)||^2_2 + \frac{1}{\sigma^2_e} ||U^T_{02}(A_1 x_1 + e)||^2_2 \]  \hspace{1cm} (4.34)

\[
= \frac{1}{\sigma^2_e} ||U^T_{02}A_1 x_1 + W^T_{1,02}e||^2_2 + \frac{1}{\sigma^2_e} ||U^T_{02}e||^2_2. \]  \hspace{1cm} (4.35)

Now from proposition \( \|U^T_{02}A_1 x_1\|_2 \geq \sqrt{\frac{1 - 2\varepsilon}{1 - \varepsilon}} \|x_1\|_2. \) We assume that \( \sqrt{\frac{1 - 2\varepsilon}{1 - \varepsilon}} \|x_1\|_2 > \|W^T_{1,02}e\|_2. \) Otherwise there is nothing left to prove. We note that \( \|W^T_{1,02}e\|_2 = \|e_{01,02}\|_2 \leq \|\mathbf{\bar{e}}_1\|_2. \) Thus,

\[
\gamma_2(S_{02}) \geq \frac{1}{\sigma^2_e} \left( \sqrt{\frac{1 - 2\varepsilon}{1 - \varepsilon}} \|x_1\|_2 - \|\mathbf{\bar{e}}_1\|_2 \right)^2 + \frac{1}{\sigma^2_e} \|e_{01,02}\|_2^2. \]  \hspace{1cm} (4.36)

Also,

\[
\gamma_3(S_{01}) - \gamma_3(S_{02}) = (|S_1| - |S_2|) \ln \frac{1 - p}{p}. \]  \hspace{1cm} (4.37)

Now since \( S_{02} = \tilde{S}, \gamma(S_{02}) \leq \gamma(S_{01}). \) Thus, from (4.22), (4.23), (4.27), (4.36) and (4.37),

\[
|S_2| \left( \ln \left( 1 + \frac{\sigma^2_1}{\sigma^2_e} \right) \left( \frac{1 - 2\varepsilon}{1 - \varepsilon} \right) \right) + 2 \ln \frac{1 - p}{p} + \left( \sqrt{\frac{1 - 2\varepsilon}{1 - \varepsilon}} \|x_1\|_2 - \|e_1\|_2 \right)^2 \]  \hspace{1cm} (4.38)

\[
\leq |S_1| \left( \ln \left( 1 + \frac{\sigma^2_1}{\sigma^2_e} (1 + \varepsilon) \right) + 2 \ln \frac{1 - p}{p} \right) + \|e_{01,02}\|_2^2 + \|e_0\|_2^2 + \frac{2(1 + \varepsilon)}{(1 - \varepsilon)\sigma^2_1} + \frac{2\|e_0\|_2^2}{\sigma^2_e} \]
Thus, exceeding $1 - \epsilon$.

Since $|S_2| \geq 0$ and $p < 1/2$ for sparse signals, the first term is non-negative. Hence,

$$\left(\sqrt{\frac{1-2\epsilon}{1-\epsilon}} \| x_1 \|_2 - \| \hat{e}_1 \|_2 \right)^2 \leq S_1 \left( \ln \left( 1 + \frac{\sigma_1^2}{\sigma_e^2} (1 + \epsilon) \right) + 2 \ln \frac{1-p}{p} \right) + \frac{2(1 + \epsilon) \| z_{01} \|_2^2}{(1-\epsilon) \sigma_1^2} + \frac{2 \| \hat{e}_{01} \|_2^2}{\sigma_e^2} + \frac{\| e_{01} \|_2^2 - \| e_{012} \|_2^2}{\sigma_e^2}.$$

(4.39)

Now $\| e_{01} \|_2^2 - \| e_{012} \|_2^2 \leq \| \hat{e}_2 \|_2^2 \leq \| e_2 \|_2^2$. Now consider the expression $\frac{\| e_{01} \|_2^2}{\sigma_e^2}$. Note that $e_{01} = \bar{U}_{01}^T e$ is the projection of $e$ onto the $|S_{01}|$-dimensional subspace $A_{01}$.

Thus $e_{01} \sim \mathcal{N}(0, \sigma_e^2 I_{|S_{01}|})$.

Let $\bar{e}_{01} = [\bar{e}_{01}, \bar{e}_2, \ldots, \bar{e}_{2|2Np-|S_{01}|}]$ such that $e_{01} \sim \mathcal{N}(0, \sigma_e^2 I_{2Np})$. By proposition $\|ar{e}_{01}\|_2^2 \leq \| \bar{e}_{01} \|_2^2 \leq 2\beta Np\sigma_e^2$ with probability exceeding $1 - e^{-Np(\beta - 1 - \ln \beta)}$ for $\beta > 1$. Similarly $\| z_{01} \|_2^2 \leq 2\beta Np\sigma_1^2$ with probability exceeding $1 - e^{-Np(\beta - 1 - \ln \beta)}$ and $\| \hat{e}_2 \|_2^2 \leq 2\beta Np\sigma_e^2$ probability exceeding $1 - e^{-Np(\beta - 1 - \ln \beta)}$.

Therefore with probability exceeding $1 - 3e^{-Np(\beta - 1 - \ln \beta)}$,

$$\left(\sqrt{\frac{1-2\epsilon}{1-\epsilon}} \| x_1 \|_2 - \| \hat{e}_1 \|_2 \right)^2 \leq C|S_1| + 4 \left(\frac{1+\epsilon}{1-\epsilon}\right) \beta Np + 4\beta Np + 2\beta Np \quad (4.40)$$

$$\leq 2CNp + 8\beta Np + 4\beta Np + 2\beta Np = (14\beta + 2C)Np, \quad (4.41)$$

since $\epsilon \leq 1/3$. Thus,

$$\sqrt{\frac{1-2\epsilon}{1-\epsilon}} \| x_1 \|_2 \leq \| \hat{e}_1 \|_2 + \sqrt{(14\beta + 2C)Np\sigma_e} \leq (\sqrt{2\beta} + \sqrt{14\beta + 2C})\sqrt{Np\sigma_e}. \quad (4.42)$$

Since $\epsilon \leq 1/3$, we can write $\| x_1 \|_2 \leq \sqrt{2(\sqrt{2\beta} + \sqrt{14\beta + 2C})\sqrt{Np\sigma_e}}$. This holds with overall probability exceeding $(1 - e^{-Np(2\ln 2 - 1)})(1 - 3e^{-Np(\beta - 1 - \ln \beta)})$ for $\beta > 1$.

4.3.3 Proof of Theorem 2

Similar to theorem 1, we assume that event $E$ i.e., $|S_{01}| \leq 2Np$ is true. This holds with probability exceeding $1 - e^{-Np(2\ln 2 - 1)}$. For the rest of the proof all events and probabilities are conditioned on this event.
Here we show that if $\mu_1$ and $\sigma_1$ satisfy the condition stated in theorem $2$ then $\gamma(S_{02})$ cannot be smaller or equal to $\gamma(S_{01})$ unless $S_1 = S_2 = \emptyset$. We obtained upper bound on $\gamma(S_{01})$ and lower bound on $\gamma(S_{02})$ in the proof of theorem $1$. If the lower bound is greater than the upper bound then we reach a contradiction that $\gamma(S_{02})$ cannot be the estimate of $S$. This happens when the inequality in (4.38) is reversed, i.e., if

$$|S_2| \left( \ln \left( 1 + \frac{\sigma_1^2}{\sigma_e^2} \left( \frac{1 - 2\epsilon}{1 - \epsilon} \right) \right) + 2 \ln \frac{1 - p}{p} \right) + \frac{\left( \sqrt{\frac{1 - 2\epsilon}{1 - \epsilon}} \|x_1\|_2 - \|\bar{e}_1\|_2 \right)^2}{\sigma_e^2} + \frac{\|e_{012}\|_2^2}{\sigma_e^2} > |S_1| \left( \ln \left( 1 + \frac{\sigma_1^2}{\sigma_e^2} (1 + \epsilon) \right) + 2 \ln \frac{1 - p}{p} \right) + \frac{\|e_{011}\|_2^2}{\sigma_e^2} + \frac{2(1 + \epsilon) \|z_{01}\|_2^2}{(1 - \epsilon)\sigma_1^2} + \frac{2\|\bar{e}_{01}\|_2^2}{\sigma_e^2} \quad (4.43)$$

Thus the following inequality is sufficient for $\gamma(S_{02})$ to be true,

$$\left( \sqrt{\frac{1 - 2\epsilon}{1 - \epsilon}} \|x_1\|_2 - \|\bar{e}_1\|_2 \right)^2 > |S_1| \left( \ln \left( 1 + \frac{\sigma_1^2}{\sigma_e^2} (1 + \epsilon) \right) + 2 \ln \frac{1 - p}{p} \right) + \frac{\|e_{011}\|_2^2}{\sigma_e^2} + \frac{2(1 + \epsilon) \|z_{01}\|_2^2}{(1 - \epsilon)\sigma_1^2} + \frac{2\|\bar{e}_{01}\|_2^2}{\sigma_e^2} \quad (4.44)$$

This is equivalent to,

$$\left( \sqrt{\frac{1 - 2\epsilon}{1 - \epsilon}} \|x_1\|_2 - \|\bar{e}_1\|_2 \right)^2 > |S_1| \left( \ln \left( 1 + \frac{\sigma_1^2}{\sigma_e^2} (1 + \epsilon) \right) + 2 \ln \frac{1 - p}{p} \right) + \frac{\|e_{011}\|_2^2 - \|e_{012}\|_2^2}{\sigma_e^2} + \frac{2(1 + \epsilon) \|z_{01}\|_2^2}{(1 - \epsilon)\sigma_1^2} + \frac{2\|\bar{e}_{01}\|_2^2}{\sigma_e^2} \quad (4.45)$$

We have seen in the proof of theorem $1$ that the right hand side is bounded above by $(14\beta + 2C)Np$ with probability exceeding $1 - 3e^{-NP(\beta - 1 - \ln \beta)}$. Thus if

$$\|x_1\|_2 > \sqrt{2}(\sqrt{2\beta} + \sqrt{14\beta + 2C})\sqrt{Np\sigma_e}, \quad (4.46)$$

(4.45) is satisfied with probability exceeding $1 - 3e^{-NP(\beta - 1 - \ln \beta)}$. Now for sufficiently large $|\mu_1|$, $\|x_1\|_2 = \|\mu_11_1 + z_1\|_2 \geq \|\mu_11_1\|_2 - \|z_1\|_2 \geq (|\mu_1| - \sqrt{\beta} \sigma_1)\sqrt{|S_1|}$ with
probability exceeding $1 - e^{-|S_1|/(\beta - 1 - \ln \beta)}$. If $|S_1| \geq 1$, then $\gamma(S_{02})$ becomes greater than $\gamma(S_{01})$ with probability exceeding $1 - 3e^{-Np(\beta - 1 - \ln \beta)} - e^{-|S_1|/(\beta - 1 - \ln \beta)}$ if,

$$|\mu_1| > \sqrt{\beta \sigma_1} + \sqrt{2}(\sqrt{2\beta} + \sqrt{14\beta + 2C})\sqrt{Np\sigma_c},$$

(4.47)

Hence $|S_1| = 0$ i.e., the set $S_1$ is empty and $S_{01} = S_0$. Thus (4.47) is a probabilistic sufficient condition that no active coefficient is missing. Now we assume that (4.47) is satisfied and we investigate what (additional) condition guarantees no false alarm with very high probability. We assume $S_2$ is not empty and find out the condition on $\mu_1$ and $\sigma_1$ that contradicts this assumption.

$$\gamma_1(S_{02}) \geq \gamma_1(S_{01}) + |S_2| \left(1 + \frac{\sigma^2_1}{\sigma^2_c} \left(\frac{1 - 2\varepsilon}{1 - \varepsilon}\right)\right),$$

(4.48)

and,

$$\gamma_3(S_{02}) = \gamma_3(S_{01}) + |S_2| \ln \frac{1 - p}{p}.$$  

(4.49)

Since set $S_1$ is empty,

$$\gamma_1(S_{01}) \leq \frac{||e_0 + A_0z_0||^2_2}{(1 - \varepsilon)\sigma^2_1 + \sigma^2_c} + \frac{||e_0||^2_2}{\sigma^2_c}.$$  

(4.50)

In obtaining (4.31) from (4.30) we lower bounded the first term by zero. Now we use a tighter lower bound by explicitly using the condition that $\mu_1 \neq 0$.

$$\gamma_2(S_{02}) = (y - \mu_1 A_{02}1_{02})^T \hat{U}_{02}^T (\sigma^2_1 \Sigma_{02} \Sigma_{02}^T + \sigma^2_c I_{02})^{-1} \hat{U}_{02}^T (y - \mu_1 A_{02}1_{02})$$

$$+ \frac{1}{\sigma^2_c} ||\hat{U}_{02}^T (y - \mu_1 A_{02}1_{02})||^2_2.$$  

(4.51)

Here $y = A_0x_0 + e$. Thus $\hat{U}_{02}^T (y - \mu_1 A_{02}1_{02}) = \hat{U}_{02}^T e = e_{02}$. Let $\hat{W}_{0/2}$ and $\hat{W}_{2/0}$ be the orthonormal bases for the orthogonal subspaces $A_0 \setminus A_2$ and $A_2 \setminus A_0$ respectively.
Thus,

\[
\gamma_2(S_{02}) \geq \frac{\| \tilde{U}_{02}^T (y - \mu_1 A_{02} 1_{02}) \|^2}{(1 + \varepsilon) \sigma_1^2 + \sigma_e^2} + \frac{\| e_{02} \|^2}{\sigma_e^2} \quad (4.52)
\]
\[
\geq \frac{\| \tilde{W}_{02}^T (y - \mu_1 A_{02} 1_{02}) \|^2}{(1 + \varepsilon) \sigma_1^2 + \sigma_e^2} + \frac{\| e_{02} \|^2}{\sigma_e^2} \quad (4.53)
\]
\[
= \frac{\| \tilde{W}_{02}^T (A_{0} z_0 + \tilde{e}_0) \|^2}{(1 + \varepsilon) \sigma_1^2 + \sigma_e^2} + \frac{\| e_{02} \|^2}{\sigma_e^2} \quad (4.54)
\]
\[
= \frac{\| \tilde{W}_{02}^T (A_{0} z_0 + \tilde{e}_0) \|^2}{(1 + \varepsilon) \sigma_1^2 + \sigma_e^2} + \frac{\| e_{02} \|^2}{\sigma_e^2} \quad (4.55)
\]
\[
\geq \frac{(1 - 2 \varepsilon)}{(1 - \varepsilon^2)} \left( \frac{1}{(1 - \varepsilon) \sigma_1^2 + \sigma_e^2} - \frac{1}{(1 + \varepsilon) \sigma_1^2 + \sigma_e^2} \right) \quad (4.56)
\]

The last inequality follows from proposition 2. Noting that \( \| e_0 \|^2 - \| e_{02} \|^2 = \| e_{2,0} \|^2 \leq \| e_2 \|^2 \),

\[
\gamma_2(S_{02}) - \gamma_2(S_{01}) \geq \left( \frac{1 - 2 \varepsilon}{1 - \varepsilon^2} \right) \left( \frac{1}{(1 - \varepsilon) \sigma_1^2 + \sigma_e^2} - \frac{1}{(1 + \varepsilon) \sigma_1^2 + \sigma_e^2} \right) \quad (4.57)
\]

Now the last term

\[
\| A_{0} z_0 + \tilde{e}_0 \|^2 \left[ \frac{1}{(1 - \varepsilon) \sigma_1^2 + \sigma_e^2} - \frac{1}{(1 + \varepsilon) \sigma_1^2 + \sigma_e^2} \right] \quad (4.58)
\]
\[
< \| A_{0} z_0 + \tilde{e}_0 \|^2 \left[ \frac{1}{(1 - \varepsilon) \sigma_1^2 + \sigma_e^2} - \frac{1}{(1 + \varepsilon) \sigma_1^2 + \sigma_e^2} \right] \quad (4.59)
\]
\[
= \frac{\varepsilon (4 + \varepsilon)}{(1 - \varepsilon)(1 + \varepsilon)^2} \frac{\| A_{0} z_0 + \tilde{e}_0 \|^2}{\sigma_1^2 + \sigma_e^2} \leq 4 \left[ \frac{\varepsilon (4 + \varepsilon)}{(1 - \varepsilon)(1 + \varepsilon)^2} \right] \beta N p < 6 \beta N p. \quad (4.60)
\]

since \( \frac{\varepsilon (4 + \varepsilon)}{(1 - \varepsilon)(1 + \varepsilon)^2} < \frac{3}{2} \) for \( \varepsilon \leq \frac{1}{3} \). Also, \( \| e_2 \|^2 / \sigma_e^2 \leq 2 \beta N p \). Then from (4.57) and (4.60),

\[
\gamma_2(S_{02}) - \gamma_2(S_{01}) \geq \left( \frac{1 - 2 \varepsilon}{1 - \varepsilon^2} \right) \left( \frac{1}{(1 + \varepsilon) \sigma_1^2 + \sigma_e^2} - 8 \beta N p \quad (4.61)
\]
Thus from (4.48), (4.49), and (4.61),
\[
\gamma(S_{02}) - \gamma(S_{01}) \geq |S_2| \left[ \frac{1}{2} \left( 1 + \frac{\sigma_1^2}{\sigma_e^2} \left( \frac{1-2\varepsilon}{1-\varepsilon} \right) \right) + \ln \frac{1-p}{p} \right] \\
+ \frac{1}{2} \frac{1-2\varepsilon}{1-\varepsilon^2} \frac{\|\bar{e}_2 - \mu_1 \mathbf{A}_2 \mathbf{1}_2\|^2}{(1+\varepsilon)\sigma_1^2 + \sigma_e^2} - 4\beta N p. \quad (4.62)
\]

The coefficient of the term $|S_2|$ is positive for sparse problems when $p \leq \frac{1}{2}$. Then for any positive value of $|S_2|$, we reach a contradiction to the assumption that $S_{02}$ is the estimate if
\[
\frac{1}{2} \frac{1-2\varepsilon}{1-\varepsilon^2} \frac{\|\bar{e}_2 - \mu_1 \mathbf{A}_2 \mathbf{1}_2\|^2}{(1+\varepsilon)\sigma_1^2 + \sigma_e^2} > 4\beta N p. \quad (4.63)
\]

Since $\varepsilon \leq \frac{1}{3}$, it is sufficient to reach a contradiction that,
\[
\|\bar{e}_2 - \mu_1 \mathbf{A}_2 \mathbf{1}_2\|^2 \geq 32\beta N p \sigma_1^2 + 24\beta N p \sigma_e^2. \quad (4.64)
\]

We note that $32\beta N p \sigma_1^2 + 24\beta N p \sigma_e^2 < (4\sqrt{2}\beta N p \sigma_1 + 2\sqrt{6}\beta N p \sigma_e)^2$ and $\|\bar{e}_2\|_2 \leq \sqrt{2\beta N p \sigma_e}$. Thus if $|S_2| \geq 1$, and
\[
|\mu_1|(1-\varepsilon) > \sqrt{2\beta N p \sigma_e} + 4\sqrt{2\beta N p \sigma_1} + 2\sqrt{6\beta N p \sigma_e} \quad (4.65)
\]
\[
= 4\sqrt{2\beta N p \sigma_1} + (1 + 2\sqrt{3})\sqrt{2\beta N p \sigma_e} \quad (4.66)
\]

then $\gamma(S_{02})$ cannot be smaller than or equal to $\gamma(S_{01})$. Thus $S_2$ must be empty. Since $\varepsilon \leq \frac{1}{3}$, a probabilistic sufficient condition for no false alarm is
\[
|\mu_1| > 6\sqrt{2\beta N p \sigma_1} + 3 \left( \frac{1}{2} + \sqrt{3} \right) \sqrt{2\beta N p \sigma_e}, \quad (4.67)
\]

which holds with probability exceeding $1 - 3e^{-Np(\beta-1-\ln \beta)}$. \qed

4.4 Discussion

From theorem 1 we see that the energy of the true signal restricted to the missed coefficients is of the order of energy in the projection of noise onto the subspace
spanned by the true signal. A natural question that arises is what can we say about the estimate of the signal \( \hat{x} \) obtained by regressing with the measurement matrix restricted to the columns indexed by \( \hat{S} \)? We mention here that \( \hat{x} \) is not an optimal estimate of \( x \) like MAP or MMSE estimates obtained directly from the observed data. Now \( \hat{x} \) is given by

\[
\hat{x} = \arg \min_{x \in \mathbb{R}^N} \| y - Ax \|_2^2.
\]

(4.68)

and it can be easily shown that

\[
\hat{x}_S = \hat{x}_{02} = (A_{02}^T A_{02})^{-1} A_{02}^T y = V_{02} \Sigma_{02}^{-1} \bar{U}_{02}^T (A_0 x_0 + A_1 x_1 + e)
\]

(4.69)

Now \( \| V_{02} \Sigma_{02}^{-1} \bar{U}_{02}^T A_1 x_1 \|_2 \leq \frac{1}{\sqrt{1-\varepsilon}} \sqrt{\frac{\varepsilon}{1-\varepsilon}} \| x_1 \|_2 \leq \frac{\varepsilon}{1-\varepsilon} K_1 \sqrt{N} p \sigma_e \) and \( \| V_{02} \Sigma_{02}^{-1} \bar{U}_{02}^T e \|_2 \leq \sqrt{\beta} \sqrt{N} p \sigma_e \). Also \( \| x_1 - \bar{x}_1 \|_2 = \| x_1 \|_2 \leq K_1 \sqrt{N} p \sigma_e \). Thus \( \| \hat{x} - x \|_2 \leq k \sqrt{N} p \sigma_e \) with probability exceeding \( (1-e^{-N p (2 \ln 2 - 1)}) (1-3 e^{-N p (\beta - 1 - \ln \beta)}) \), where \( k = \left( \frac{K_1}{1-\varepsilon} + \sqrt{\frac{\beta}{1-\varepsilon}} \right) \).

This is optimal in the sense that even if the true support was known it is not possible to do any better. This also shows that even if there is any coefficient \( i \) falsely detected, due to the restricted isometry property, its estimate \( \hat{x}_{\{i\}} \) must be small.

Let us analyze the values of the constants appearing in the theorem statements. Consider the example where \( N = 4096, p = 0.01, M = 256, \mu_1 = 0 \) and nominal SNR \( 10 \log \frac{N p \sigma_1^2}{M \sigma_e^2} = 20 \) dB. Then for \( \beta = 1.6, K_1 = 12.94 \) and the probability is at least 0.9854 and for \( \beta = 2, K_1 = 13.77 \) and the probability is at least \( 1-1.06 \times 10^{-5} \). So the constants are modest for reasonable values of the system parameters. Fig. 4.1 shows the plots of the constant \( K_1 \) and the lower bound of the probability as functions of the parameter \( \beta \) for this example. For the same values of \( N, M, p \) and \( \sigma_1^2, \sigma_e^2 \), theorem 2 gives the value of \( K_2 \) needed to obtain the lower bound on the absolute value of the
Fig. 4.1: The plot in the upper panel shows the constant $K_1$ as a function of the parameter $\beta$. Here $N = 4096, p = 0.01, M = 256, \mu_1 = 0$ and nominal SNR $10\log_{10}\frac{Np\sigma^2}{M\sigma^2_e} = 20$ dB. The figure in the bottom panel shows the least probability with which the energy in the missed coefficients is upper bounded by $K_1^2 Np\sigma^2_e$.

mean $\mu_1$ to probabilistically guarantee perfect support recovery. If $\beta = 1.6, \bar{\beta} = 16$, then $K_3 = 10.75\sqrt{Np}, K_4 = 12.94\sqrt{2Np}$ and the probability is at least 0.9832 and if $\beta = 2, \bar{\beta} = 25$, then $K_3 = 12.01\sqrt{Np}, K_4 = 13.77\sqrt{2Np}$ and the probability is at least $1 - 4.13 \times 10^{-5}$.

From the statement of theorem 4.1 we see that the constant $K_1$ depends on $C = \ln(1 + \frac{\sigma_1^2}{\sigma_2^2})$. The term $\frac{\sigma_1^2}{\sigma_2^2}$ is related to SNR. We see from Fig. 4.1 that with SNR the constant $K_1$ increases. So if the SNR increases in an unbounded fashion keeping the noise energy constant then does the energy in the missed support grows unbounded? The answer is no. If $\sigma_1$ becomes very large then irrespective of the value of $\mu_1$, the probability that any element of $x$ is close to zero and suppressed by noise becomes very small and every element is detected with high probability. From (4.40) we can
see that
\[
\left( \sqrt{1 - 2\varepsilon} \frac{\|x_1\|_2 - \|\bar{e}_1\|_2}{\sigma_e^2} \right)^2 \leq C|S_1| + 8\beta Np + 4\beta Np + 2\beta Np. 
\] (4.71)

If $|S_1| \neq 0$, the left hand side grows as $\frac{\sigma^2_1}{\sigma_e^2}|S_1|$ whereas the right hand side grows as $\ln\left(\frac{\sigma^2_1}{\sigma_e^2}\right)|S_1|$. Thus as SNR grows very large, set $S_1$ has to be empty and there is no missed coefficient with very high probability. Therefore the upper bound stated in theorem 1 is loose in the very high SNR regime. For any practical value of the SNR the term $\ln(1 + \frac{\sigma^2_1}{\sigma_e^2})$ has a moderate value. Hence the constant $K_1$ is a reasonably small constant.

In order to obtain simple expressions in the theorem statements we have used the inequality $\varepsilon \leq \frac{1}{3}$ instead of having $\varepsilon$ appearing in those expressions. As a consequence the constants in the results show the worst case scenarios when $\varepsilon = \frac{1}{3}$. Proceeding in a similar way, for other values of the RIP constant we can obtain tighter constant values in our results.
CHAPTER 5

PARAMETRIC MODEL FOR SPECTRAL-SPATIAL EPR IMAGING

5.1 Introduction

The existing spectral-spatial imaging techniques are hampered by long collection times due to large sweep widths, large number of projections and by missing projection angles. In this work, we explicitly use prior knowledge of the lineshape functional form, such as Lorentzian, to address these deficiencies. Spectral-spatial EPR measurements are modeled as a function of spin density and lineshape parameters at each spatial location. Object properties are inferred from the data by maximum a posteriori probability (MAP) estimation. With no reliance on backprojection for inversion, the approach suffers no artifacts from missing projection angles, arbitrarily spaced sampling of gradient strength or spectral truncation. The estimation framework directly accounts for the decrease in SNR versus gradient strength, provides a principled means of selecting gradient strengths for acquisition, and reports noise sensitivity of estimated parameters. Simulation and experimental results demonstrate that reliable reconstruction is possible from two projections and a spectral window that is only equal to the maximum spectral linewidth. Additional projections or increased sweep
width provide increased robustness to measurement noise. The proposed technique is
described for two-dimensional spectral-spatial imaging and can be extended to higher
dimensions.

The material of this chapter is based on:

S. Som, L.C. Potter, R. Ahmad, and P. Kuppusamy,
“A Parametric Approach to Spectral-spatial EPR Imaging”

Summary of the results has also been published as:

S. Som, L.C. Potter, R. Ahmad, and P. Kuppusamy,
“Reduced Acquisition EPR Oximetry”
A Joint Conference of 12th In Vivo EPR Spectroscopy and Imaging, and

5.2 Data Model

In this section, a mathematical model is formulated to describe the spectral-spatial
EPR measurements in terms of the unknown spin density and spectral profile. For
clarity and simplicity of presentation, one spatial dimension is considered here.

5.2.1 Parametric Object Model

Let the spatial dimension be denoted by $y$. The field of view (FOV) $L$ is discretely
approximated as $K$ uniformly spaced piece-wise constant intervals numbered by $k$
from $-K/2$ to $K/2 - 1$. For interval $k$, the lower and upper endpoints $y_{l,k}$ and $y_{u,k}$
are given by

$$y_{l,k} = k \frac{L}{K} \quad \text{and} \quad y_{u,k} = (k + 1) \frac{L}{K}. \tag{5.1}$$
On each interval, the spectral dimension, denoted by $h$, is assumed to have a Lorentzian lineshape. The spin density and Lorentzian half-linewidth (i.e., half width at half maximum) in the $k^{th}$ interval are denoted by $d_k$ and $\tau_k$, respectively. The center of the Lorentzian is assumed to be known, constant, and equal to $h_0$ for every interval. Thus, the spectral-spatial object model is given by

$$S(y, h) = \frac{d_k \tau_k}{(h - h_0)^2 + \tau_k^2}, \quad y_{l,k} \leq y < y_{u,k}. \quad (5.2)$$

Let $d$ and $\tau$ denote the lists of $K$ spin densities and $K$ half-linewidths specifying the object model, and define $\xi = [d \, \tau]^T$ to be the column vector of the $2K$ parameters.

5.2.2 Parametric Projection Model

The geometry of a 2D spectral-spatial projection is depicted in Fig. 5.1. A static gradient field is used to create a pseudo angle $\alpha$, where $\frac{\sqrt{2} \Delta H}{\cos \alpha}$ is the sweep-width and $\Delta H$ is the spectral window; the maximum pseudo angle $\alpha_{\text{max}}$ relates to the physical maximum gradient $G_{\text{max}}$ by $L = \tan(\alpha_{\text{max}}) \Delta H / G_{\text{max}} \quad [64]$. The normal distance of the line of integration from the origin of the pseudo object is denoted by $s$. The line of projection (AB) is given by

$$h = y \frac{\Delta H}{L} \tan \alpha + \frac{s}{\cos \alpha}, \quad (5.3)$$

and it intersects the lower and upper edges of the $k^{th}$ segment at positions $y_{l,k}$ and $y_{u,k}$, respectively. The corresponding $h$ co-ordinates are

$$h_{l,k}(s, \alpha) = y_{l,k} \frac{\Delta H}{L} \tan \alpha + \frac{s}{\cos \alpha}, \quad (5.4)$$

$$h_{u,k}(s, \alpha) = y_{u,k} \frac{\Delta H}{L} \tan \alpha + \frac{s}{\cos \alpha}. \quad (5.5)$$
Fig. 5.1: In spectral-spatial imaging, line integrals are measured through a pseudo object by first applying a static magnetic field gradient, then sweeping the main (uniform) magnetic field to excite electron magnetic moments. Here, the vertical axis is the spatial axis and the horizontal axis is the spectral axis. The spatial axis is normalized to make the FOV same as the spectral window $\Delta H$; $\gamma = \Delta H/L$ is the normalizing constant.
The projection $P(s, \alpha; \xi)$ is given by the line integral

$$P(s, \alpha; \xi) = \frac{c}{\sin \alpha} \sum_{k=-K}^{K-1} \int_{h_{u,k}(s,\alpha)}^{h_{l,k}(s,\alpha)} \frac{d_k \tau_k}{(h-h_0)^2 + \tau_k^2} dh,$$

(5.6)

where $c$ is a calibration constant. Note that the projection lines are not truncated by any spectral window; therefore, the model does not suffer the approximation error introduced in inverse Radon transform reconstruction by neglecting contribution from area under the tails of the spectral lineshape outside the spectral window.

If the modulation amplitude and frequency are small, then the measured data $f(s, \alpha; \xi)$ due to Zeeman modulation are proportional to the first derivative of $P(s, \alpha; \xi)$ with respect to $s$ and are scaled by a factor of $\cos^2 \alpha$.

$$f(s, \alpha; \xi) = \tilde{c} (\cos^2 \alpha) \frac{\partial}{\partial s} P(s, \alpha; \xi) = \tilde{c} \sum_{k=-K}^{K-1} \frac{d_k \tau_k}{\tan \alpha} \left( \frac{1}{(h_{u,k}(s,\alpha) - h_0)^2 + \tau_k^2} - \frac{1}{(h_{l,k}(s,\alpha) - h_0)^2 + \tau_k^2} \right),$$

(5.7)

where $\tilde{c}$ is the revised calibration constant.

If $N$ samples are taken at every angle, then $s$ may be replaced by sample number $n$ in Eq. (5.7) using

$$s = \sqrt{2} \Delta H n \frac{n}{N}, \quad n = -N/2, \ldots, N/2 - 1.$$

(5.8)

Substitution of eqns. (5.1) and (5.8) into eqns. (5.7), (5.4) and (5.5) yields

$$f(n, \alpha; \xi) = \frac{\tilde{c}}{\tan \alpha} \sum_{k=-K}^{K-1} d_k \tau_k \left( \frac{1}{(h_{u,k}(n,\alpha) - h_0)^2 + \tau_k^2} - \frac{1}{(h_{l,k}(n,\alpha) - h_0)^2 + \tau_k^2} \right),$$

$$h_{l,k}(n, \alpha) = k \Delta H \frac{\tan \alpha + \sqrt{2} \Delta H n}{N \cos \alpha},$$

$$h_{u,k}(n, \alpha) = (k+1) \Delta H \frac{\tan \alpha + \sqrt{2} \Delta H n}{N \cos \alpha}.$$
Note that by application of L'Hôpital's rule to Eq. \[5.9\], the zero gradient projection case, \(i.e., \alpha = 0\), gives

\[
f(n, 0; \xi) = \frac{2\tilde{c}\Delta H}{K} \sum_{k=-\frac{K}{2}}^{\frac{K}{2} - 1} d_k \tau_k \left( h_0 - \frac{\sqrt{2}\Delta H n}{N} \right) \right) \left( \left( \frac{\sqrt{2}\Delta H n}{N} - h_0 \right)^2 + \tau_k^2 \right).
\]

(5.10)

5.2.3 Noise Model

Measurement noise is modeled as additive, zero mean, Gaussian, and uncorrelated with variance \(\sigma^2\). Let \(\mathbf{Y}\) denote the measurements, with samples from all angles concatenated. Thus, \(\mathbf{Y}\) is a multi-variate Gaussian random vector with mean \(\mathbf{f}\) and diagonal covariance matrix \(\sigma^2 \mathbf{I}\).

Given this parametric model, spectral-spatial imaging is the task of inferring parameters \(d\) and \(\tau\) from the noisy observations, \(\mathbf{Y}\).

5.3 Parameter Estimation

A Bayesian approach is adopted for parameter estimation and yields a regularized least-squares inversion. A confidence measure for estimated parameters is determined using the Cramèr-Rao lower bound.

5.3.1 Maximum A Posteriori Probability (MAP) Estimate

The parameter vector \(\xi\) is estimated by maximizing the posterior probability of \(\xi\) given the noisy measurements, \(\mathbf{Y}\). Invoking Bayes’ formula,

\[
\hat{\xi} = \arg \max_{\xi} p(\xi | \mathbf{Y}) = \arg \max_{\xi} \frac{p(\mathbf{Y} | \xi) p(\xi)}{p(\mathbf{Y})}
\]

\[
= \arg \min_{\xi} \left\{ \log p(\mathbf{Y} | \xi) + \log p(\xi) \right\}
\]

\[
= \arg \min_{\xi} \frac{1}{2\sigma^2} \sum_{n, \alpha} \left( Y(n, \alpha) - f(n, \alpha; \xi) \right)^2 + g(\xi).
\]

(5.11)
The prior probability density \( p(\xi) \propto \exp\{-g(\xi)\} \) is used to encode prior knowledge of the spectral-spatial object. We adopt

\[
g(\xi) = \sum_{k=-K/2}^{K/2-2} \lambda_d (d_{k+1} - d_k)^2 + \lambda_r (\tau_{k+1} - \tau_k)^2.
\]  

(5.12)

to express the belief that smooth distributions of spin density and half-linewidth are likely.

For decreasing \((\lambda_d, \lambda_r)\) and fixed measurement noise power \(\sigma^2\), the MAP estimate allows less smoothness and enforces greater fidelity to the noisy measurements. Here, we adopt \(2\sigma^2\lambda_r = 2\sigma^2\lambda_d = \lambda\), assuming the dynamic range of numerical magnitudes of \(d_k\) and \(\tau_k\) to be of the same order; this can be achieved either by choosing appropriate units of \(d_k\) and \(\tau_k\) or by scaling \(d_k\) and absorbing the scaling factor into \(\tilde{c}\). Multiplying the cost function of Eq. [5.11] by \(2\sigma^2\) yields

\[
\hat{\xi} = \arg \min_{\xi} \sum_{n,\alpha} \left( Y(n, \alpha) - f(n, \alpha; \xi) \right)^2 + \lambda \sum_{k=-K/2}^{K/2-2} (d_{k+1} - d_k)^2 + (\tau_{k+1} - \tau_k)^2.
\]  

(5.13)

The function \(g(\xi)\) alternatively may be viewed as a regularization term added to the least-squares cost. Roughness penalties are commonly adopted for image reconstruction and restoration to combat oscillation in least-squares solutions: see, e.g., [126, 127] and references therein.

### 5.3.2 Numerical optimization

The optimization task in Eq. [5.13] may be solved by many numerical methods; we use the interior-reflective Newton method implemented in the Matlab\(^3\) 7.1 routine.

\(^3\)Matlab is a registered trademark of The Mathworks, Inc., Natick, MA, USA
lsqnonlin. Note that the cost function is quadratic in $d$ but non-convex in $\tau$. Further, the gradient of the cost function is easily computed. The iterative optimization algorithm is initialized at $d_k = 0$ and $\tau_k = \tau_{\text{min}}$ for each $k$, where $\tau_{\text{min}} > 0$ is a minimum physically meaningful half-linewidth. In addition, the spin density is constrained by $d_k \geq 0$ and half-linewidth by $\tau_{\text{min}} \leq \tau_k \leq \tau_{\text{max}}$.

### 5.3.3 Cramér-Rao Bound on Error Variance

The Cramér-Rao bound (CRB) gives a lower bound on the parameter estimation error variance for any unbiased estimator [125]. We use the CRB to calculate the posterior confidence interval for estimated parameters. The bound is obtained by inverting the Fisher information matrix, $I_F$

$$
\mathbf{E}[(\hat{\xi} - \xi)(\hat{\xi} - \xi)^T] \geq I_F^{-1},
$$

where $\mathbf{E}$ denotes expectation, the left-hand side is the $2K$-by-$2K$ error covariance matrix, and the inequality $A \geq B$ denotes that the matrix difference $A - B$ is non-negative definite.

In the Bayesian estimation framework, the Fisher information matrix $I_F$ is the sum of two terms: $I_M$ due to measurements and $I_P$ from the prior information [125], where the $(i, j)^{th}$ elements of $I_M$ and $I_P$ are given by

$$
I_{Mij} = -\mathbf{E} \left[ \frac{\partial^2 \ln p(Y|\xi)}{\partial \xi_i \partial \xi_j} \right],
$$

and

$$
I_{Pij} = -\mathbf{E} \left[ \frac{\partial^2 \ln p(\xi)}{\partial \xi_i \partial \xi_j} \right].
$$

Fisher information describes the local curvature of the log-likelihood function and admits an intuitive interpretation. At parameter values for which the log-likelihood
has low curvature (i.e., is relatively flat), the cost function in Eq. 5.13 is not sensitive to small changes in the estimated parameters; hence, the estimation error variance due to measurement noise is relatively large. In contrast, where the log-likelihood function has high curvature, the cost is sensitive to small changes in the estimated parameters, resulting in low variance parameter estimates.

In section 5.5, the proposed imaging procedure is applied to measured data collected from nitroxide solutions using an L-band spectrometer. As prelude, section 5.4 explores two questions via computer simulation. First, what is the sensitivity of parameters to perturbations in measured data? Second, which projection angles are most informative?

5.4 Simulation Results

The data model postulated in section 6.2 and inversion procedure described in section 5.3 are examined via numerical simulations. Synthetic experiments are used to evaluate sensitivity to local minima, to quantify sensitivity to additive measurement noise, to study polynomial correction of baseline drift, to explore selection of projection angles, and to evaluate selection of regularization constant.

Simulation results are reported for the piece-wise constant phantom shown in Fig. 5.2. The Lorentzian peak location is $h_0 = 1 \text{ G}$. For sections 5.4.1 and 5.4.2, the simulation parameters are: spectral window $\Delta H = 3 \text{ G}$, $K = 32$ spatial segments, $N = 256$ samples per projection angle and two projections at $\alpha = -83.1^\circ$ and $-69.2^\circ$.

One goal in simulation is to evaluate the relative information content of different projection angles. Therefore, $\lambda$ is set to zero to avoid any confounding influence from the smoothness prior, $p(\xi)$. 

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5.4.1 Convexity and Initialization

Numerical experience suggests that local minima do not pose a hazard to the nonconvex optimization in Eq. (5.13). To test sensitivity to initialization, the optimization routine was executed for 100 random initializations, \(d_k\) uniform on \([0, 1]\) and \(\tau_k\) uniform on \([0.05, 0.9]\), \(k = -16, ..., 15\). Fig. 5.2 shows the superimposed estimated \(d_k\) and \(\tau_k\) for 100 random initializations. The signal-to-noise ratio (SNR) was set at 30 dB, where SNR is defined as the ratio of signal power to noise power. The maximum, across all \(k\) and all trials, of observed variance of spin density \((d_k)\) estimates is \(3.3 \times 10^{-7}\) and that of half-linewidth \((\tau_k)\) estimates is \(8.5 \times 10^{-7}\). The maximum, across \(k\), of absolute deviation from the mean estimate for \(d_k\) is 0.0027 and for \(\tau_k\) is 0.0044.

5.4.2 Bias and Variance

The spin density and half-linewidth were estimated from 500 different noise realizations. The mean estimation error for \(d_k\) has a maximum absolute value of \(2.6 \times 10^{-3}\) across \(k\) and the same for \(\tau_k\) is \(2.8 \times 10^{-3}\) at 30 dB SNR. Thus, the mean estimation errors are negligible.

Fig. 5.3 displays simulated error standard deviation of half-linewidth \((\tau_k)\) from 500 different noise realizations, along with the corresponding Cramér-Rao bound. The figure illustrates the efficacy of the theoretical bound to characterize noise sensitivity. Two themes are seen which are likewise observed for other synthetic phantoms: uncertainty in lineshape increases for lower spin density, and uncertainty decreases away from the center of the FOV.
Fig. 5.2: 1D spatial phantom with $K = 32$ and piece-wise constant spin density and half-linewidth (dashed lines). Estimated $d_k$ and $\tau_k$ (solid lines) from 100 random initializations and for a fixed noise realization at 30 dB ($\sigma = 0.0051$). The 100 estimated profiles are superimposed.
Fig. 5.3: Theoretical bound and simulated (from 500 trials) error standard deviations for half-linewidths $\tau_k$. 
5.4.3 Angle Selection

The Cramer-Rao bound can also inform selection of projection angles. Fig. 5.4 shows the CRB for error standard deviation of the $d_2$ and $\tau_2$ parameters versus angle of projection for the object shown in Fig. 5.2. The graphs illustrate the two opposing effects of higher gradient strengths. On one hand, higher gradient, hence higher projection angle, yields more informative projections. On the other hand, the higher gradient yields lower SNR. The two effects combine in Fig. 5.4 to give minimum parameter error at a high angle near 80 degrees. To explore a combination of projection angles, Fig. 5.5 displays the CRB for various pairs of angles and shows that $(80, 60)$ is preferred over the nearly complementary angle pair $(85, 5)$. This CRB sensitivity analysis can only be computed for a known object; nonetheless, it was observed that the error bounds for many objects show the same trends as found in Fig. 5.4 and Fig. 5.5. Thus studying the CRB for simulated objects can guide the selection of projection angles to be collected in practice.

5.4.4 Selection of Regularization Constant

To explore dependence of reconstruction error on the parameter $\lambda$, simulations were run at SNR values from 15 dB to 35 dB in 5 dB steps. Reconstructions were computed for $\lambda$ in the set $\{0, 0.0001, 0.001, 0.01, 0.1, 1\}$. The root mean square error (RMSE) was averaged from 50 trials at each combination of SNR and $\lambda$. Over the range of SNR values considered, selection of $\lambda$ from the three orders of magnitude $\{0.001, 0.01, 0.1\}$ yields similar RMSE; no more than 3.6% difference was observed. Thus a wide range of $\lambda$ values is found to give similar reconstruction results.
Fig. 5.4: Cramér-Rao bound of the spin density $d_2$ and half-linewidth $\tau_2$ versus angle of projection $\alpha$. 
Fig. 5.5: Cramér-Rao bound for the spin density $d_k$ and half-linewidth $\tau_k$ for various combinations of angles of projection $\alpha$. 
With decreasing SNR, the RMSE increases; and the value of $\lambda$, yielding lowest RMSE is SNR dependent. The choice $\lambda = 0.1$ yielded lowest RMSE for SNR values of 20, 25 and 30 dB. Expectedly, at lower SNR, $\lambda$ should be increased to reflect the reduced fidelity of the measured data.

### 5.4.5 Baseline Drift Correction

Since the sweep-width is of the order of linewidth of the Lorentzian, the standard baseline drift correction method on the measured data after integration cannot be applied directly in the proposed approach. Instead a polynomial model of the baseline is added to the forward projection model and the parameters of the polynomial at each projection angle are estimated from the measured data. Simulation showed that if a baseline drift of 20% of the output signal peak per Gauss is introduced, then the average RMSE of $\tau$ from 50 trials is 43% at 30 dB SNR when baseline drift in not included in the model. But if a baseline drift model is used, then the the average RMSE drops to 5%. Fig. 5.6 shows a typical reconstruction result from projections with baseline drift.

### 5.5 Experimental Results

An experiment was performed to validate the proposed technique and its performance. Lineshape is characterized, spin density and half-linewidth are estimated from measured data, the residual between measured data and model fit is analysed, and Cramér-Rao bounds are reported.

The phantom shown in Fig. 5.7 was constructed from three tubes with inner diameter of 2.75 mm each and outer diameter of 4.0 mm. Tubes were filled with
Fig. 5.6: Projections with and without baseline drift and true and estimated parameters. The data with baseline drift were used for parameter estimation. A linear baseline correction model on the unmodulated projection was assumed and the same correction model gives a constant drift correction in the modulated projection model. At the $-83.1^\circ$ projection the drift is positive and at $-69.2^\circ$ projection the drift is negative. The SNR value is 25 dB and the regularization constant $\lambda = 0.1$. 
<table>
<thead>
<tr>
<th>Concentrations</th>
<th>% fit err</th>
<th>fit err (dB)</th>
<th>( \tau ) (Gauss)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 mM</td>
<td>5.2%</td>
<td>-25.7 dB</td>
<td>0.35</td>
</tr>
<tr>
<td>0.8 mM</td>
<td>4.7%</td>
<td>-26.5 dB</td>
<td>0.71</td>
</tr>
<tr>
<td>0.5 mM</td>
<td>5.2%</td>
<td>-25.7 dB</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Table 5.1: Characterization results of solutions used in the phantom. The spin densities in the three tubes are proportional to the solution strengths. The half-linewidths are obtained from Lorentzian curve-fit to the zero gradient projections obtained for the three solutions.

three different concentrations (1.0, 0.8, and 0.5 mM from left to right) of \(^{15}\text{N-PDT (4-Oxo-2,2,6,6-tetramethyl-piperidine-d}_{16}^{15}\text{N-oxy)} radical dissolved in distilled water. Chromium oxalate (CrOx) in distilled water was used as a broadening agent. The concentrations of CrOx in the three solutions were 0, 2.33 and 0.65 mM respectively. A detailed discussion on CrOx induced linebroadening is given elsewhere [128].

5.5.1 Lineshape Characterization

To characterize the lineshape function, the absorption signal from each tube was measured separately using an L-band (1.2 GHz) EPR spectrometer. The Lorentzian curve-fit for the 0.5 mM solution is shown in Fig. 5.8. The results of curve-fit for all three solutions are summarized in Table 5.1. The fit error is defined as the ratio of the norm of residual to the norm of measured lineshape.

5.5.2 Spectral-spatial Imaging

Imaging was carried out with a reentrant resonator of diameter of 12.6 mm and a useable height of 12 mm. Results are reported in sections 5.5.3, 5.5.4 and 5.5.5 for the following spectrometer settings: incident power 4 mW; spectral window \( \Delta H = 1.4 \) G;
Fig. 5.7: The phantom used for experiment. Top-left: Photograph of the phantom; the three tubes are glued together and filled with nitroxide solutions with three different concentrations mixed with different amounts of the broadening agent. Bottom-left: Schematic of the cross-section of the inner perimeters of the tubes. The magnetic field gradient is along the horizontal axis. Top-right: Spin density profile. Bottom-right: Half-linewidth profile.
Fig. 5.8: Measured zero gradient projection of the 0.5 mM solution and the best-fit Lorentzian. The fit error is 5.2%.
spatial field of view $L = 14.14$ mm; modulation amplitude 0.2 G; modulation frequency 100 kHz. Various spectrometer settings gave consistent reconstruction results. A total of 13 projections were acquired. Each acquired projection had 4096 data points which were downsampled to 256 points. No corrections for baseline or B1 field inhomogeneities [129] were applied.

5.5.3 Parameter Estimation

Spin density and half-linewidth are estimated using Eq. [5.13], and the reconstructed object is shown in Fig. 5.9, the estimated spin density and estimated half-linewidth are shown in the Fig. 5.10. Two angles of projection, $-83.1^\circ$ (8.3 G/cm) and $-69.2^\circ$ (2.6 G/cm), are used, and the proportionality constant $\tilde{c}$ is chosen so that the spin densities $d_k$ have approximately the same range of values as the half-linewidths $\tau_k$. The modulation gave a measured PSNR of 14.4 in the $-83.1^\circ$ projection and 63.6 for the $-69.2^\circ$ projection, where PSNR is the ratio of the peak signal to the peak noise. The total acquisition time for these two projection angles is 59.3 s. In the numerical optimization, $\lambda = 0.01$, $\tau_{min} = 0.3$ G and $\tau_{max} = 0.9$ G. The computation time is 4.14 s 4.46 s on a Pentium® D 2.6 GHz processor with 2 GB RAM.

5.5.4 Residual Analysis

The noise assumptions are examined by analysis of the residual. The residual, $Y(n, \alpha) - f(n, \alpha; \xi)$, is the fit error between the measured data and the estimated parametric model in Eq. [5.9]. Fig. 5.11 shows the measured projection and the fit error. The observed signal-to-noise ratio is 32.5 dB. A Lilliefors test, with 0.05 level of significance, accepts the hypothesized Gaussian distribution, $p = 0.15$. 74
Fig. 5.9: Reconstructed spectral-spatial object from experimental data. Two angles of projections at $-83.1^\circ$ and $-69.2^\circ$, with 256 samples at each angle, are used. The regularization coefficient is $\lambda = 0.01$. The spectral window, $\Delta H$, is 1.4 G, and the maximum linewidth of the Lorentzian present is 1.4 G.
Fig. 5.10: Top-left: Reconstructed spin density ($d_k$) values from experimental data. Bottom-left: Reconstructed half-linewidth ($\tau_k$) values. Top-right: Cramér-Rao bounds for estimation error standard deviations of $d_k$. Bottom-right: Cramér-Rao bounds for estimation error standard deviations of $\tau_k$. The $d_k$ and $\tau_k$ estimates are accepted if the CRB is less than 10 times the minimum of CRB across all $k$, otherwise they are discarded and not shown in the left column $d_k$ and $\tau_k$ plots.
Fig. 5.11: Measured data and residual fit error. Top-left: The measured data at $-83.1^\circ$. Top-right: Measured data at $-69.2^\circ$. Bottom-left: 10 times the residual fit error at $-83.1^\circ$. Bottom-right: 10 times the residual fit error at $-69.2^\circ$. The vertical axis is in arbitrary unit and the horizontal axis denotes sample number.
5.5.5 Cramér-Rao Bound

Cramér-Rao bounds for estimation error standard deviations of $d_k$ and $\tau_k$ are computed using $\hat{\xi}$ and $\hat{\sigma}^2$, where $\hat{\xi}$ is the estimated parameter vector and $\hat{\sigma}^2$ is the measured variance of the residual. The bounds are shown in Fig. 5.10. The standard deviation of $\tau_k$ estimation error is high between the tubes where there is no spin density. If the error standard deviation is less than 10 times the minimum of CRB across all $k$, then the estimated values are accepted and are otherwise discarded. Note that this reliability analysis shows only the effect of additive measurement noise and does not take into account the effects of magnetic field inhomogeneity or error introduced by deviation of lineshapes from the functional form in Eq. [5.2].

5.6 Comparison with Projection-reprojection Method

Performance of a projection-reprojection method [65] was analysed using a simulated tube phantom similar to the one used for the experiment. The use of simulation was necessitated by the inability of our spectrometer to measure the wide sweep width required to follow the published guidelines suggested for projection-reprojection. Fig. 5.12 shows the reconstruction results from the projection-reprojection and parametric approaches. For the parametric method the spectral window and projection angles reported in section 5.5 were again used. With simulated noise of 30 dB SNR the reconstruction error for $\tau$ was 5.4% using the two projection angles and $\lambda = 0$. The corresponding data acquisition time is 59.3 s, assuming a sweep rate of 0.19 G/s and a main field recovery time of 1 sec.

For the projection-reprojection method, the data acquisition and algorithm parameters were varied in an attempt to obtain the lowest reconstruction error with the
least acquisition time. The spectral window was 14.1 times the maximum linewidth present; 15 projection angles were used, uniformly spaced from $-81^\circ$ to $81^\circ$. An additional 16 angles were used for reprojection, 14 of which were selected at the midpoints between the measured angles, and $-85.5^\circ$ and $85.5^\circ$ angles were selected at the high gradient region. The PSNR for the zero gradient projection was equivalent for the two methods. The reconstruction error for $\tau$ after six iterations was 18.6%. The corresponding data acquisition time for the reprojection imaging is 37.83 min.

Thus, for this phantom the parametric approach required 38 times less data acquisition time compared to the projection-reprojection method and yielded lower reconstruction error.

5.7 Discussion

The proposed parametric estimation approach offers significant reduction in data acquisition time for spectral-spatial EPR imaging. The savings come from both a small spectral window and a low number of projections. In comparison to tomographic reprojection methods for the examples considered, the reduced sweep width and reduced number of projections combine to yield 30 : 1 to 40 : 1 reduction in data acquisition time for equal or lower reconstruction error.

The maximum a posteriori probability estimation approach adopted in Eq. 5.13 reduces to maximum likelihood (ML) estimation for regularization parameter $\lambda = 0$. For Gaussian noise, the ML estimate is the nonlinear least squares curve fit. A nonzero $\lambda$ reduces the oscillatory artifacts seen in a least squares solution. The estimation procedure is not sensitive to the choice of $\lambda$; for the experimental data in Section 5.5.
Fig. 5.12: Reconstructed spin density and half-linewidth by projection-reprojection and parametric methods.
values of $\lambda$ across three orders of magnitude, $0.01 \leq \lambda \leq 1$, give similar reconstruction results.

Higher error at the center of the FOV is observed in both simulation and measurement. Physically, consider the line integrals through the pseudo-object that yield the samples near either end of a projection. These line integrals depend on only a few spatial locations, and therefore have contribution from only a few unknown values of spin density and line width. Consequently, parameters at the ends of the 1D spatial object are less sensitive to estimation error.

The proposed imaging approach is a direct inversion of the measured data using a regularized nonlinear regression. Unlike tomographic approaches, no approximation error is introduced by truncation of the lineshape by the spectral window. The estimation procedure is applicable for any set of arbitrarily spaced projection angles and is not handicapped by the missing angle artifact introduced by tomographic inversion. Additionally, the estimation approach directly and explicitly incorporates into the inversion the noise properties of the spectral-spatial measurements. In contrast, in tomographic processing with magnetic field modulation, numerical integration to obtain projection data introduces strong noise correlation, and backprojection disregards the high variability in PSNR that is due to the $\cos^2 \alpha$ scaling shown in Eq. [5.7].

The model-based inversion exploits prior knowledge that the spectral lineshapes are from a parametric family of functions. Using the model in Eq. [5.2], the number of unknowns in a $K \times K$ image is reduced from $K^2$ to $2K$. Moreover, as illustrated in Fig. 5.1 every sample from each projection angle contains information from every spatial location, thereby permitting recovery of the spin density and linewidth from
a single projection in the noiseless case. Additional projections provide increased robustness to measurement noise and modeling imperfections.

The lineshape model in Eq. 5.2 may be extended from Lorentzian to any parametric function, such as a mixture of Lorentzians with unknown central locations, or the convolution of a Gaussian with a Lorentzian.

A strength of the proposed processing procedure is the explicit identification of the physical assumptions adopted in its derivation. This transparency allows informed judgment concerning the suitability of the technique for any candidate application.

5.8 Conclusion

A parameter estimation framework for spectral-spatial EPR imaging is presented. The approach provides reliable reconstruction of spin density and spectral linewidth with an order of magnitude reduction in data acquisition time, compared to tomographic inversion. The proposed technique is suitable for any application in which spectral lineshapes under study can be accurately approximated as members of a parametric family of functions. The imaging procedure was demonstrated using computer simulation and measurements on an experimental phantom.
6.1 Introduction

We present a method for EPR oximetry in three spatial dimensions using a particulate probe. The technique provides estimates of the location, extent, spin density and Lorentzian linewidth of each discrete probe implant. Each probe implant is a small collection of spins encapsulated in an oxygen permeable lattice; an implant is assumed to experience a constant partial pressure of oxygen across its extent. The shape of the implant is arbitrary and may be irregular from one implant to the next. As in other CW spectral-spatial imaging techniques, data is collected by varying the direction and strength of an applied magnetic gradient field. The proposed data processing exploits the sparseness of spin probe implants to detect voxels with nonzero spin and to estimate the spectral linewidth for each implant.

Each spatial voxel is characterized by an unknown spin density and linewidth. Further, each projection has unknown main magnetic field drift and linear baseline drift. These parameters are estimated jointly from a small set of projections. The sparseness of the probe implants implies that spin density is zero at most voxels,
which in turn makes the nonlinear estimation problem a stable and tractable numerical task. The parsimonious representation of sparse spin locations and associated probe implant linewidths permits orders of magnitude reduction in the number of acquired projections, compared to four-dimensional reconstruction of an arbitrary spectral-spatial object. A small sweep width is employed, relative to widths required for 4D backprojection or Fourier imaging, further reducing acquisition time. The estimation procedure does not require that implant lineshapes are resolved in any single projection.

The material of this chapter is based on:

S. Som, L.C. Potter, R. Ahmad, D.S. Vikram, and P. Kuppusamy,
“EPR Oximetry in Three Dimensions using Sparse Spin Distribution”

Summary of the results has also been published as:

S. Som, L.C Potter, R. Ahmad, D.S. Vikram, and P. Kuppusamy,
“Rapid EPR Oximetry Using Sparse Spin Distribution”

6.2 Data Model

In this section, a mathematical model is formulated to describe the 4D spectral-spatial EPR measurements in terms of the unknown spin density and spectral profile.
6.2.1 Forward Model for 4D Spectral-spatial EPR Imaging

Magnetic resonance spectra measured using static linear magnetic field gradients may be viewed as projections of an object with an intrinsic spectral dimension [130, 131, 132]. Following previous 4D spectral-spatial developments [90], we describe the acquired spectra in terms of the Radon transform of a spectral-spatial object, assuming a small amplitude Zeeman modulation and lock-in detection of the absorption first harmonic. Our 4D forward model is an extension of the 2D model described in [53].

The forward data model is formulated by discretizing the three spatial dimensions into voxels and treating the spectral dimension as continuous. Let the spatial dimensions be denoted by \((x, y, z)\) and the spectral dimension by \(h\). The field of view (FOV) \(L\) along any spatial dimension is discretely approximated as \(K\) uniformly spaced piece-wise constant intervals. Throughout this and subsequent sections it is assumed that the lineshape is a Lorentzian.

Consider voxel \(k\) whose boundaries along the three dimensions are \(x_p, x_{p+1}, y_q, y_{q+1}, z_r, z_{r+1}\) and let \(d_k\) and \(\tau_k\) be the spin density and half-width at half maximum (HWHM) respectively at that voxel location. The 4D spectral-spatial object at voxel location \(k\) can be written as,

\[
F(x, y, z, h) = \frac{d_k\tau_k}{(h - h_d)^2 + \tau_k^2},
\]

for \(x_p \leq x < x_{p+1}, y_q \leq y < y_{q+1}, z_r \leq z < z_{r+1}\. \tag{6.1}
\]

where \(h \in [-\Delta H/2, \Delta H/2]\), \(\Delta H\) being the spectral window, and \(h_d\) is the main magnetic field drift in the instrument which is the difference between the main magnetic field and the resonance field. It is assumed that \(h_0\) is constant over the entire FOV.
Moreover if the instrument is known to be stable i.e., no magnetic field drift occurs, then \( h_d \) can be considered as known and equal to zero.

We describe the 4D spectral-spatial data acquisition in the spherical polar coordinate system \((s, \eta, \phi, \theta)\) defined by

\[
\begin{align*}
x &= s \sin \theta \sin \phi \cos \eta \\
y &= s \sin \theta \sin \phi \sin \eta \\
z &= s \sin \theta \cos \phi \\
h &= s \cos \theta.
\end{align*}
\] (6.2)

Here \((\eta, \phi)\) define the spatial orientation of the magnetic field gradient and \(s\) gives the uniform sweep field. The pseudo angle \(\theta\) is related to the magnitude of the magnetic field gradient by

\[
G = \tan \theta \times \Delta H/L,
\] (6.3)

where \(G\) is the applied gradient strength. The range of \(\theta\) is assumed to be \((-\frac{\pi}{2}, \frac{\pi}{2})\).

The 4D Radon transform of the object is obtained by integrating the spectral-spatial object \(F(x, y, z, h)\) along the hyper-plane

\[
s = ((x \cos \eta + y \sin \eta) \sin \phi + z \cos \phi) \sin \theta + h \cos \theta.
\] (6.4)

The same hyper-plane can be written as

\[
h = \frac{s}{\cos \theta} - ((x \cos \eta + y \sin \eta) \sin \phi + z \cos \phi) \tan \theta.
\]

We define \(f(x, y, z) \equiv h\ i.e.,\)

\[
f(x, y, z) = \frac{s}{\cos \theta} - ((x \cos \eta + y \sin \eta) \sin \phi + z \cos \phi) \tan \theta.
\]
The differential volume \[133\] of the spectral-spatial object \( F(x, y, z, h) \) through this hyper-surface is given by

\[
dV = F(x, y, z, h) \sqrt{1 + f_x^2 + f_y^2 + f_z^2} \mathrm{d}x \mathrm{d}y \mathrm{d}z,
\]  

(6.5)

where \( f_x = \frac{\partial f(x,y,z)}{\partial x} \), \( f_y = \frac{\partial f(x,y,z)}{\partial y} \) and \( f_z = \frac{\partial f(x,y,z)}{\partial z} \). Thus the 4D Radon transform of \( F(x, y, z, h) \) is obtained by adding the contributions from all voxels and is given by,

\[
P(\eta, \phi, \theta, s) = \int dV
\]

\[
= \int \int \int F(x, y, z, h) \sqrt{1 + f_x^2 + f_y^2 + f_z^2} \mathrm{d}x \mathrm{d}y \mathrm{d}z
\]

\[
= \frac{1}{\cos \theta} \sum_k \sum_{x=x_p}^{x_{p+1}} \sum_{y=y_q}^{y_{q+1}} \sum_{z=z_r}^{z_{r+1}} F(x, y, z, h) \mathrm{d}x \mathrm{d}y \mathrm{d}z. \quad (6.6)
\]

If the Zeeman modulation amplitude, \( B_m \), is small, then the measured output is well approximated by the first harmonic absorption spectrum \[133\] and is given by the first derivative of the 4D Radon transform scaled by \( \cos^2 \theta \). Carrying out the integration in Eq. \( \text{6.6} \) and then differentiating with respect to \( s \),

\[
\tilde{P}(\eta, \phi, \theta, s) = \sum_k \frac{d_k \tau_k}{abc e^2} \left[ \frac{1}{\tau_k} \left\{ -v_1 \tan^{-1} \left( \frac{v_1}{\tau_k} \right) 
\right.
\right.
\]

\[
+ v_2 \tan^{-1} \left( \frac{v_2}{\tau_k} \right) + v_3 \tan^{-1} \left( \frac{v_3}{\tau_k} \right) + v_4 \tan^{-1} \left( \frac{v_4}{\tau_k} \right) 
\]

\[
- v_5 \tan^{-1} \left( \frac{v_5}{\tau_k} \right) - v_6 \tan^{-1} \left( \frac{v_6}{\tau_k} \right) + v_7 \tan^{-1} \left( \frac{v_7}{\tau_k} \right) 
\]

\[
- v_8 \tan^{-1} \left( \frac{v_8}{\tau_k} \right) \} + \frac{1}{2} \left\{ \ln(1 + \left( \frac{v_1}{\tau_k} \right)^2) - \ln(1 + \left( \frac{v_2}{\tau_k} \right)^2)
\right.
\]

\[
- \ln(1 + \left( \frac{v_3}{\tau_k} \right)^2) - \ln(1 + \left( \frac{v_4}{\tau_k} \right)^2) + \ln(1 + \left( \frac{v_5}{\tau_k} \right)^2)
\]

\[
+ \ln(1 + \left( \frac{v_6}{\tau_k} \right)^2) - \ln(1 + \left( \frac{v_7}{\tau_k} \right)^2) + \ln(1 + \left( \frac{v_8}{\tau_k} \right)^2) \} \right], \quad (6.7)
\]
where,

\[
\begin{align*}
  a &= \cos \eta \sin \phi \tan \theta \quad (6.8) \\
  b &= \sin \eta \sin \phi \tan \theta \quad (6.9) \\
  c &= \cos \phi \tan \theta \quad (6.10) \\
  e &= \cos \theta \quad (6.11) \\
  v_1 &= (cz_{r+1} + by_q - \frac{s}{e} + ax_p + h_d) \quad (6.12) \\
  v_2 &= (cz_{r+1} + by_{q+1} - \frac{s}{e} + ax_{p+1} + h_d) \quad (6.13) \\
  v_3 &= (cz_{r+1} + by_q - \frac{s}{e} + ax_{p+1} + h_d) \quad (6.14) \\
  v_4 &= (cz_{r} + by_{q+1} - \frac{s}{e} + ax_{p+1} + h_d) \quad (6.15) \\
  v_5 &= (cz_{r} + by_q - \frac{s}{e} + ax_{p+1} + h_d) \quad (6.16) \\
  v_6 &= (cz_{r} + by_{q+1} - \frac{s}{e} + ax_{p} + h_d) \quad (6.17) \\
  v_7 &= (cz_{r} + by_q - \frac{s}{e} + ax_{p} + h_d) \quad (6.18) \\
  v_8 &= (cz_{r+1} + by_{q+1} - \frac{s}{e} + ax_{p+1} + h_d). \quad (6.19)
\end{align*}
\]

The first harmonic absorption from Zeeman modulation thus becomes,

\[
Y_z(\eta, \phi, \theta, s) = B_m \cos^2 \theta \tilde{P}(\eta, \phi, \theta, s) \quad (6.20)
\]

Note that it is assumed in Eq. 6.7 through Eq. 6.20 that \(\eta\) and \(\phi\) are not integer multiples of \(\pi/2\). The limiting cases for these singularities can be obtained by application of L'Hôpital’s rule to the corresponding equations.

To complete the data model, three parameters are included for each projection: a linear approximation to baseline drift, \(\alpha s + \beta\), and a magnetic field drift, \(h_d\). The magnetic field drift is assumed unknown, but fixed, for each projection and is allowed
to vary independently from projection to projection. Thus the measured output can be written as

\[ Y(\eta, \phi, \theta, s) = Y_z(\eta, \phi, \theta, s) + \alpha(\eta, \phi, \theta)s + \beta(\eta, \phi, \theta) + N(\eta, \phi, \theta, s) \]  

(6.21)

where \( N(\eta, \phi, \theta, s) \) is zero mean additive white Gaussian measurement noise with variance \( \sigma^2 \). Also in Eq. [6.12] through Eq. [6.19] \( h_d \) becomes \( h_d(\eta, \phi, \theta) \).

Eq. [6.21] gives a generic model for 4D spectral-spatial imaging where each voxel can have different spin density and linewidth. For the proposed approach we assume that the linewidth is constant within any implant but the spin density can vary within it. This reduces the number of unknown linewidth parameters to the number of implants present.

In summary, the spin density at every voxel, linewidth for each implant, the baseline drift for each projection, and the magnetic field drift for each projection comprise the unknown parameters in the data model.

6.3 Sparse Imaging

In this section, we describe the data processing procedures for estimating implant locations and linewidths.

We assume particulate paramagnetic probe implants are introduced to the region of interest and fill only a small fraction of the field of view. Each implant is small and is assumed to experience a constant \( pO_2 \) across the implant. For example, in the experiment presented in Section [6.4] four implants, each approximately 2 mm\(^3\), are placed in an 8000 mm\(^3\) FOV. EPR spectra are collected for 32 different projections. The model given in Eq. [6.21] describes measured EPR spectra as a function of several
unknowns. The parameters to be estimated from the noisy spectra are: spin density for each voxel occupied by an implant; one linewidth for each implant; and three calibration parameters for each projection – a magnetic field drift, a baseline drift, and a baseline offset.

In three spatial dimensions, the number of variables in the nonlinear parametric model grows very large and beyond the ability of numerical methods to directly find the minimum error solution. To reduce the dimensionality, we find initial estimates of implant locations by adopting a linearized model with homogeneous lineshape. The linear model allows simple use of sparseness of the implants within the field of view. For example, with $128 \times 128 \times 128$ voxels and 128 projections, the curve fit requires 4.19 million unknowns, including parameters for baseline drift and unknown magnetic field drift for each projection. But, with 8 implants each filling, on average, an irregular volume of 128 voxels, a 4000:1 reduction is obtained in the number of free variables.

The initial estimate is computed as a sparse solution to the linear model using $\ell_1$-penalized least-squares, as discussed below. This convex optimization task is computationally simple. The initial probe sites are biased by blurring due to the incorrect, but convenient, assumption of homogeneous lineshape in the linearized model. In the second step, the bias is removed and the linewidths are estimated by applying the nonlinear model in Eq. [6.21] to the full 3D volume, but with regions of zero spin having been identified by the initialization. Hence, the curve fit in 3D is computable using a gradient descent method. Note that the shapes and the exact sizes of implants are unknown in this approach.
Thus, the complexity and non-convexity of the large nonlinear regression encountered in three spatial dimensions are overcome by using a linearized model to detect the approximate locations of the unknown implants.

6.3.1 Sparse Initialization

To detect regions of nonzero spin using only a few projections, we temporarily assume a spatially-invariant imaging model and employ a sparse reconstruction technique. That is, we assume a fixed homogeneous linewidth throughout the FOV and construct a blurred image. A reconstructed spin density map is sought having very few non-zero voxels. Computation of sparse solutions to underdetermined linear equations has been a topic of considerable recent interest \[135,136,137,138,139,121\]. For simplicity, we adopt the technique of Gradient Projection Sparse Reconstruction \[140\], which solves

\[
\min_d \frac{1}{2} \| y - A d \|^2 + \lambda \sum_i d_i \quad \text{s.t.} \quad d \geq 0.
\]

Here, \( y \) represents the list of all measured data samples and \( d \) is the list of non-negative spin densities for all voxels. The matrix \( A \) is computed from Eq. \[6.20\], using a fixed linewidth and magnetic field drift. The first term in Eq. \[6.22\] gives the error between the data and the model and the second term gives \( \lambda \) times the \( \ell_1 \) norm of the spin density vector \( d \). The \( \ell_1 \) norm of a vector is the summation of absolute values of all the elements; here the absolute value is same as the value of the element since spin densities are constrained to non-negative numbers. We select the sparsity parameter \( \lambda \) according to

\[
\lambda = 0.1 \| A^T y \|_\infty
\]

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as suggested in [140]. However, we have observed that values of $\lambda$ ranging about an order of magnitude give very similar results in the problems considered.

From the reconstructed spin density map, we use the \texttt{clusterdata} routine from Matlab 7.1 to cluster the voxels into candidate regions corresponding to the individual implants. The centroid of each region is used to identify candidate nonzero voxels; specifically, voxels inside a sphere with radius twice the maximum extent of an implanted probe are detected for further processing. Thus, the sparse initialization serves merely to safely discard many voxels with zero spin, thereby dramatically reducing the dimensionality and complexity of the nonlinear curve fitting task.

### 6.3.2 Gradient Descent

Armed with a list of candidate non-zero voxels, the model in Eq. [6.21] is used to estimate the unknown parameters. A nonlinear least-squares fit is computed using the \texttt{lsqnonlin} routine from Matlab 7.1; note that the derivative of the model with respect to each parameter is readily computable from Eq. [6.21], and used in \texttt{lsqnonlin} to provide a gradient descent method. Unknown parameters are initialized to $d = 0$, $\tau = \tau_{\text{min}}$, $\alpha = \beta = 0$, where $\tau_{\text{min}}$ is the minimum feasible value of $\tau$. The initial value for magnetic field drift, $h_d$, for each projection is the average from the zero gradient projections taken before and after the data collection.

\textsuperscript{4}Matlab is a registered trademark of The Mathworks, Inc., Natick, MA, USA.
Fig. 6.1: Schematic of tube construction. Tube was filled with lithium octa-n-butoxy naphthalocyanine (LiNc-BuO) up to a height of 3-5 mm; different amounts of Na$_2$S$_2$O$_4$ and water were used to obtain variation in linewidth.

Fig. 6.2: Left: Four capillary tubes used as phantom consisting of 4 probes. Right: The phantom inside the L-Band (1.2 GHz) resonator.
6.4 Experimental Results

6.4.1 Experiment Design

A phantom using 50 µl capillary tubes was constructed. Each capillary tube (inner diameter 0.9 mm) was filled with lithium octa-n-butoxy naphthalocyanine (LiNc-BuO) up to a height of 3-5 mm. Each tube contained approximately $8 \times 10^{16}$ spins. Variations in linewidths were obtained by using different amounts of sodium hydrosulfite ($\text{Na}_2\text{S}_2\text{O}_4$) and water, a combination known for changing the oxygen concentration to which the sample will be exposed. A total of 18 capillary tubes were prepared, out of which 4 were used to construct the phantom. The four tubes were selected to provide both a large range of linewidths and a subset of closely matched linewidths. The HWHM linewidths of the spins in the tubes were estimated by least squares curve fit to the individual zero-gradient spectrum, and the characterization result is reported in Table 6.1. The tube schematic and photographs of the phantom and resonator are shown in Figs. 6.1 and 6.2.

An L-Band (1.2 GHz) EPRI system was used for data acquisition. A volume resonator with diameter 12.6 mm and sensitive height 12 mm was used. Spectrometer settings were: incident microwave power 5 mW, resonance field 457.5 G, sweep width 6 G, lock in time constant 0.01 s, modulation amplitude 0.1 G, scan rate 1.53 G/s, field of view $2 \text{ cm} \times 2 \text{ cm} \times 2 \text{ cm}$, maximum gradient strength applied 20 G/cm and corresponding maximum spectral angle $\theta = 81.47^\circ$. The four tubes were inserted into a cylindrical plastic holder that was pushed inside the cavity. In the absence of magnetic field gradient, the measured SNR was 25.2 dB and PSNR was 101.7 for the composite spectrum of the phantom consisting of four probe implants. Here SNR is defined as $20\log_{10}\left(\frac{S_S}{S_N}\right)$ where $S_S$ is the norm of the signal and $S_N$ is the norm of the
residual by least-squares curve fit to the zero gradient composite spectrum (which is considered as noise). PSNR is defined as the ratio of the peak-to-peak signal and the noise (residual) standard deviation.

Six sets of data were collected each having 32 projections. The projection angles were generated using 4D uniform distribution of points over a hypersphere [142]. For each set of angles a random initialization of projection angles was used so that projection angles corresponding to the final uniform distributions were different for each set. Since the information content of a low gradient projection is small [53], the permissible spectral angle range was selected to be $30^\circ$ to $81.47^\circ$. The upper limit is a hardware constraint on maximum gradient strength. On average each set of 32 projections required 8.8 min acquisition time.

6.4.2 Estimation of Linewidth

In the initialization stage sparse $16 \times 16 \times 16$ spin density maps were estimated. Fig. 6.4 shows the sparse spin density map for dataset 1. The matrix $A$ was explicitly calculated from Eq. [6.20]. The fixed linewidth assumed for the entire FOV was 1.0 G. The magnetic field drift $h_d$ was taken as the mean value of magnetic field drift obtained from the zero gradient projection measured at the beginning and at the end of data collection. Then four regions were identified by clustering. For the second stage a $32 \times 32 \times 32$ voxel reconstruction was computed. The spin density and linewidths were estimated for the four spherical regions with radius of 3 voxels. Final spin density and linewidth estimates are shown in Fig. 6.4. Baseline drift and magnetic field drift corrections were estimated as described in section 6.2. The characterized and estimated HWHM linewidths are provided in table 6.1. Average computation
Fig. 6.3: Three typical projection samples from the first dataset. The four lineshapes are not resolved in any of the projections. Spectrum A: $\eta = 75.01^\circ, \phi = 86.73^\circ, \theta = -81.47^\circ$, Spectrum B: $\eta = 52.55^\circ, \phi = 89.94^\circ, \theta = -51.16^\circ$ and Spectrum C: $\eta = 77.48^\circ, \phi = 45.68^\circ, \theta = -81.47^\circ$. Small sweep-width reduces data collection time and increases SNR by avoiding the tails of the spectra where the signal strength is very low.
<table>
<thead>
<tr>
<th>Dataset</th>
<th>Probe 1 G (mmHg)</th>
<th>Probe 2 G (mmHg)</th>
<th>Probe 3 G (mmHg)</th>
<th>Probe 4 G (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characterization</td>
<td>0.32 (7.4)</td>
<td>0.40 (21.6)</td>
<td>0.46 (32.9)</td>
<td>1.36 (161.0)</td>
</tr>
<tr>
<td>Dataset 1</td>
<td>0.31 (6.1)</td>
<td>0.39 (19.3)</td>
<td>0.48 (36.0)</td>
<td>1.36 (160.0)</td>
</tr>
<tr>
<td>Dataset 2</td>
<td>0.32 (8.2)</td>
<td>0.39 (20.4)</td>
<td>0.45 (30.1)</td>
<td>1.44 (171.8)</td>
</tr>
<tr>
<td>Dataset 3</td>
<td>0.32 (7.8)</td>
<td>0.38 (19.0)</td>
<td>0.46 (31.8)</td>
<td>1.42 (169.0)</td>
</tr>
<tr>
<td>Dataset 4</td>
<td>0.30 (4.7)</td>
<td>0.38 (17.7)</td>
<td>0.45 (31.3)</td>
<td>1.26 (145.1)</td>
</tr>
<tr>
<td>Dataset 5</td>
<td>0.32 (7.8)</td>
<td>0.40 (21.1)</td>
<td>0.45 (31.5)</td>
<td>1.48 (178.6)</td>
</tr>
<tr>
<td>Dataset 6</td>
<td>0.29 (2.8)</td>
<td>0.37 (17.2)</td>
<td>0.41 (23.2)</td>
<td>1.42 (169.1)</td>
</tr>
<tr>
<td>RMS error</td>
<td>0.01 (2.3)</td>
<td>0.02 (4.4)</td>
<td>0.02 (2.8)</td>
<td>0.08 (11.5)</td>
</tr>
</tbody>
</table>

Table 6.1: Estimated linewidths of the implants from different datasets. The first row gives the characterization result and the last row reports the root mean square error. The values within parentheses show corresponding pO₂ values.

time was 70.3 minutes on a Pentium® D 3.2 GHz processor with 3 GB RAM. The computation time at each iteration is dominated by evaluation of the cost function, Eq. [6.21], and its derivatives. Because each data point from each projection can be independently calculated in Eq. [6.21], fast computation can be readily accomplished using parallel processors.

6.5 Discussion

The estimated linewidths reported in Gauss can be converted to pO₂ values as given in table 6.1 using the calibration curves obtained following the procedure described in [79]. The calibration curves of pO₂ vs. HWHM linewidth are linear with a slope of 0.0056 G/mmHg and intercept of 0.28 G for the first three implants and a slope of 0.0068 G/mmHg and intercept of 0.28 G for the fourth implant. The root mean square (RMS) error for the implant with the highest linewidth is significantly
Fig. 6.4: Top-left: Sparse $16 \times 16 \times 16$ reconstruction of spin density map from dataset 1. The fixed HWHM linewidth assumed was 1.0 G. Top-right: Spherical regions of 3 voxel unit radius in $32 \times 32 \times 32$ FOV whose spin density and linewidths were estimated in the second stage. The spin density was assumed to be zero outside these four regions. Bottom-left: Spin density estimates from the second stage. Bottom-right: Linewidth estimates from the second stage.
higher than the other three implants which can be attributed to the low peak-to-
peak signal from the broadest lineshape as seen in Fig. 6.5. For the three probe
implants corresponding to \( \text{pO}_2 \) of less than 33 mmHg, the RMS error is observed to
be 3.3 mmHg. For all four implants, the overall RMS error is 6.4 mmHg.

For applications in which spatially sampled \( \text{pO}_2 \) measurements provide the rele-
vant biological information, the proposed procedure yields a 4D spectral-spatial image
from very few field sweeps. While existing 4D image procedures [90, 91] use approxi-
mately 1000 field sweeps to provide maps of arbitrarily diffused spin probes, here the
explicit use of knowledge about sparseness of particulate probe implants and incor-
poration of parametric lineshape into the forward model made it possible to measure
\( \text{pO}_2 \) using 32 sweeps.

The proposed parametric estimation approach offers significant reduction in data
acquisition time for spectral-spatial EPR imaging. The savings come from both a
low number of projections and a small spectral window; in contrast, a large spectral
window is required in techniques that first invert the Radon transform before using
the Lorentzian line shape. The average data collection time for the six datasets was
8.8 min/dataset considering a 1.53 G/s scan rate. At the same scan rate considering
a spectral window of 12 times the maximum HWHM, the data collection time is 6 hrs
31 min for 512 projections generated using 4D uniform distribution of points over a
hypersphere [142]. The acquisition time reduction is more than 40:1.

The proposed imaging approach is a direct inversion of the measured data us-
ing a nonlinear regression. Unlike tomographic approaches, no approximation error
is introduced by truncation of the lineshape by the spectral window. The estima-
tion procedure is applicable for any set of arbitrarily spaced projection angles and
is not handicapped by the missing angle artifact introduced by tomographic inversion. Additionally, the estimation approach directly and explicitly incorporates into the inversion the noise properties of the spectral-spatial measurements. In contrast, in tomographic processing with magnetic field modulation, numerical integration to obtain projection data introduces strong noise correlation, and backprojection disregards the high variability in PSNR that is due to the $\cos^2 \theta$ scaling seen in Eq. [6.20].

Our approach is based on parameter estimation. The accuracy of the pO2 estimates, as quantified by the mean-squared error, is case dependent and is determined by several factors: SNR, model mismatch (field inhomogeneity, non-Lorentzian lines, etc), object geometry, and collection angles. Sensitivity of the estimated values can be predicted using the Cramèr-Rao (CR) lower bound [53]. Further, the CR bound analysis informs the choice of projection angles and the trade-off between more angles and higher SNR per angle.

For significant SNR enhancement, the proposed approach may be extended for use with large-amplitude Zeeman modulation and joint measurement [113] of absorption and dispersion. The extension requires inclusion of the absorption and dispersion components into the forward model. The over-modulation may provide approximately 3-5 times enhancement in peak signal amplitudes [91]. Likewise, joint measurement of multiple harmonics from both absorption and dispersion spectra can provide approximately four times improvement in SNR [113], with a corresponding acceleration in acquisition time. With these extensions, the proposed sparse EPR oximetry method may be viewed as combining five themes present in the literature: (i) the sparseness of particulate probes exploited by Grinberg et al. in multi-site oximetry [70]; (ii) the SNR enhancement of time-locked subsampling proposed by Hyde et al. [113]; (iii) the
Fig. 6.5: Zero gradient spectra of the four implants. The implant with the broadest lineshape has the lowest peak-to-peak signal which leads to higher estimation error as compared to the other implants.

SNR enhancement of curve fitting to over-modulated Lorentzian line shapes achieved by Elas et al. [91]; (iv) 4D localization provided by spectral-spatial imaging [90,91]; and (v) dimension reduction [53] by directly estimating Lorentzian line parameters, rather than first imaging a spectral-spatial object.
6.6 Conclusion

Despite significant advances made in recent decades, long acquisition times have hampered the wide-spread use of free radical and oxygen measurements in biological systems using EPR imaging. In the proposed method, we estimate sampled maps of pO$_2$ by sparsely introducing a particulate probe and collecting EPR spectra for a small sequence of applied magnetic gradient fields. The processing exploits two assumptions that hold for multi-site measurements: spectral lineshapes are from a parametric family of functions, and paramagnetic implants are sparse within the field of view. Resolution of estimated pO$_2$ is linewidth dependent. For a LiNc-BuO probe, the proposed processing was experimentally demonstrated with 32 projections collected at L-band with 25.2 dB zero gradient projection SNR. For enhanced SNR and hence reduced acquisition time or improved resolution, the approach is readily extensible to Zeeman over-modulation and to joint acquisition of absorption and dispersion spectra.
CHAPTER 7

DIGITAL DETECTION AND PROCESSING OF MULTIPLE QUADRATURE HARMONICS FOR EPR SPECTROSCOPY

7.1 Introduction

In this chapter, we present a direct digital receiver design and briefly outline its implementation. The receiver utilizes high-speed dual-channel analog-to-digital converter (ADC) to simultaneously sample the bandpass signals from the microwave source and the circulator which carries the reflected signal from the sample cavity. Direct digital conversion avoids noise and nonlinear distortion associated with analog mixers. Further, this configuration does not require the sampling frequency to be time-locked to the microwave reference [113]. Unlike previously reported work [116], which processed the absorption data alone, we present a framework to jointly process multiple harmonics for quadrature channels. In addition, our proposed processing is capable of handling unequal noise powers between the quadrature channels, for instance due to phase noise of the microwave source. Other benefits of the proposed receiver and processing include recovery of microwave phase and seamless handling of baseline distortion and magnetic field drifts.

The material of this chapter is based on the submission: 103

Summary of the results has also been published as:


7.2 Methodology

Digital detection offers an array of advantages over the traditional homodyne detection, including collection of multiple harmonics and flexibility of retrospective signal processing. However, implementation of a digital receiver poses unique technical challenges. In this section, we briefly overview the proposed digital receiver design, highlighting its differences from the existing designs. Also, we present a convergent iterative processing scheme for a maximum-likelihood estimation of the unknown parameters under nonideal conditions, such as in the presence of phase noise, unknown microwave phase, and baseline drift.

7.2.1 Receiver Overview

The basic operation of the direct digital receiver is summarized in Fig. 7.1. The microwave signal reflected from the sample cavity is amplified and bandpass filtered before being sampled by one of the channels, called channel 1, of the ADC. If the
sampling frequency $\omega_s$ does not meet the Nyquist criterion, the microwave signal is replicated as shown in Fig. 7.1. For a bandpass signal with bandwidth less than $\omega_s$, however, an appropriate selection of $\omega_s$ ensures that the subsampling does not introduce aliasing artifacts. The other channel, called channel 2, of the ADC is used to sample the microwave source signal at the same rate. The sampled streams from both the ADC channels are stored on a permanent storage device for further processing. Once stored, the contents of channel 1 ($C_1$) are digitally multiplied with the contents of channel 2 ($C_2$) and its Hilbert transform ($\tilde{C}_2$) to generate in-phase ($S_I$) and out-of-phase ($S_Q$) baseband channels, respectively. Both $S_I$ and $S_Q$ are then digitally cross-correlated with sinusoidal waveforms of field modulation frequency $\omega_m$ and its multiples to extract individual harmonics $I_1, I_2, I_3, \ldots$, and $Q_1, Q_2, Q_3, \ldots$, respectively. All the postprocessing is carried out on a block-by-block basis. The chosen data block size should be small enough not to violate the approximation of fixed magnetic field for each block.

7.2.2 Hardware Layout

Fig. 7.2 and 7.3 show the block diagram of the digital receiver and its interface with a CW EPR spectrometer, respectively. The microwave signal from the circulator is amplified using a 40 dB low-noise amplifier (LNA) and bandpass filtered using an analog filter with 75 MHz bandwidth before being fed to channel 1 of the ADC. The signal from the microwave source, a cavity oscillator in this case, is bandpass filtered using a similar analog filter before being fed to channel 2 of the ADC. The sampling and field modulation waveforms are phase-locked via generation by a common arbitrary waveform generator (AWG). An output from the AWG indicating the periodic
Fig. 7.1: Frequency domain illustration of digital detection. Reflected EPR signal along with the noise shown in gray (i); reflected signal after bandpass filtering (ii); sampling frequency generated by AWG (iii); sampled bandpass reflected signal (iv); sampled bandpass microwave signal from the microwave source (v); baseband signal $S_I$ (or $S_Q$, depending on the phase of microwave signal) obtained by point-by-point time-domain multiplication of iv and v (vi); sampled field modulation signal (vii); point-by-point time-domain multiplication of vi and vii (viii); digital lowpass filtering to obtain one sample of the $I_1$ (or $Q_1$) (ix). For simplicity, only one harmonic is displayed around the microwave carrier.
zero-crossing of the field modulation waveform is also fed to the ADC (connection iii in Fig. 7.3). This signal encodes the true phase of the field modulation, and is used to synthetically generate a field modulation waveform and its harmonics. The individual harmonics are extracted by matched filtering $S_I$ and $S_Q$ with the synthetically generated field modulation waveforms. Traditional AFC circuitry, employing PSD, is used to lock $\omega_c$ to $\omega_0$. The time-constant of the AFC is kept large enough to ensure that there is no AFC response to $\omega_m$ or any of its multiples. Typical design parameters for the digital receiver are summarized in Table 7.1 and specifications of the major components are reported in Table 7.2.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symbol</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microwave Frequency</td>
<td>$\omega_c$</td>
<td>$2\pi \times 1.283 \times 10^9$ rad/s</td>
</tr>
<tr>
<td>Sampling Frequency</td>
<td>$\omega_s$</td>
<td>$2\pi \times 400 \times 10^6$ rad/s</td>
</tr>
<tr>
<td>Modulation Frequency</td>
<td>$\omega_m$</td>
<td>$2\pi \times 100 \times 10^3$ rad/s</td>
</tr>
<tr>
<td>AFC Frequency</td>
<td></td>
<td>$2\pi \times 76.8 \times 10^3$ rad/s</td>
</tr>
<tr>
<td>Microwave Power</td>
<td></td>
<td>2 mW</td>
</tr>
</tbody>
</table>

Table 7.1: Typical parameter values for the designed L-band digital receiver.

No reference arm was used in our design. To bias the diode detector of the AFC, the coupling parameter $\beta_0$ was manually adjusted to induce slight overcoupling. Too much departure from the critical coupling ($\beta_0 = 1$), however, was troublesome in a number of ways. First, it decreased the overall sensitivity of the system. Second, it threatened to saturate the LNA. Lastly, it reduced the effective vertical resolution of the ADC because the EPR signal became increasingly smaller than the dynamic range of the ADC defined by the stronger microwave carrier. Therefore, the coupling was kept as close to the critical value as allowed by the AFC locking capability.
Fig. 7.2: Block diagram of CW spectrometer capable of direct digital detection.
Unlike time-locked subsampling, a strict adherence to $\omega_s$ values to generate four samples in an odd number of cycles was not required in our design. Any value of $\omega_s$ that resulted in nonoverlapping replicas of the bandpass microwave signal was a viable option. Although it was possible to use lower sampling frequency, a use of higher frequency, even when it is below the Nyquist rate, offers advantages. The most important benefit of a high sampling rate is its positive effect on the antialiasing bandpass filter design. A large value of $\omega_s$ alleviates the requirement of sharp transition from pass-band to stop-band. Also, it allows for filters with lower quality-factor, which are easier to design and possess favorable characteristics such a uniform amplitude and group delay across the bandwidth of the EPR signal. Another advantage of high $\omega_s$ is the increase in effective vertical resolution of the ADC. The only downside of
Table 7.2: Digital receiver components specifications.

<table>
<thead>
<tr>
<th>Component</th>
<th>Vendor and Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPF</td>
<td>K &amp; L Microwave (custom made), center=1.282 GHz, bandwidth=75 MHz</td>
</tr>
<tr>
<td>LNA</td>
<td>HD Communications (HD 24410), gain=40 dB</td>
</tr>
<tr>
<td>ADC</td>
<td>Ultraview Corp. (AD12-500×2-8GB), upto 500 MS/s, 12 bit vertical resolution, and 8 GB RAM</td>
</tr>
<tr>
<td>Resonator</td>
<td>Home built reentrant resonator, 12 mm diameter, 12 mm length, $\omega_0 = 1.283 \text{ GHz}$</td>
</tr>
<tr>
<td>Oscillator</td>
<td>Englemann Microwave (CC-12), cavity oscillator, $\omega_c = 1 - 2 \text{ GHz}$</td>
</tr>
<tr>
<td>Field Controller</td>
<td>Bruker ER 032M</td>
</tr>
<tr>
<td>AWG</td>
<td>Tektronix (AWG7122B)</td>
</tr>
<tr>
<td>Computer</td>
<td>Ultraview Corp., Intel dual core 2.66 GHz, 8 GB RAM, 1 TB hard drive</td>
</tr>
</tbody>
</table>

A high sampling frequency is the amount of data generated. For our design, the two ADC channels collectively generated 6 GB of data for a four second scan. Although the PCI express-based ADC board itself is capable of real-time streaming, the actual data transfer from the ADC on-board memory to the computer took 40 s, primarily due to slow write speed of the hard drive. This limitation, however, can be handled by using commercially available fast storage systems. For example, PCI express host adapter (ExpressSAS H6F0) by Atto Technology (Amherst, New York) is capable of handling up to 600 MB/s bandwidth for each of its 16 external ports.

7.2.3 Signal and Noise Model

The phase noise, defined by the random additive variations in the phase of the microwave signal, is invariably present in the output of all oscillators. Depending on the type of resonator, type of oscillator, and microwave power, the phase noise may
become the dominant noise source in the EPR spectra. Several solutions have been proposed by the EPR community to counter the effects of phase noise. Some common remedies include avoiding the phase noise prone dispersion component altogether, using a low-phase noise Gunn diode oscillator \cite{144}, using a low quality-factor loop-gap resonator \cite{112}, reducing the incident microwave power, and using a bimodal resonator \cite{145, 146}. Our approach does not eliminate or suppress the phase noise itself, but instead exploits a quadrature receiver to reliably estimate EPR lineshape parameters in the presence of phase noise. Also, the approach, which is capable of handling unknown microwave phase, is an attractive alternative to adjusting the phase by manual tuning \cite{147}.

Because the two inputs arriving at the ADC are not phase-locked, the harmonics generated by $S_I$ and $S_Q$ channels are not purely absorption and dispersion but a combination which is given by

$$
I_h(H_0) = a_h(H_0) \cos \phi_0 - b_h(H_0) \sin \phi_0
Q_h(H_0) = a_h(H_0) \sin \phi_0 + b_h(H_0) \cos \phi_0
$$

where $H_0$ represents the external magnetic field; $\phi_0$ denotes the unknown microwave phase discrepancy between the two channels of the ADC; $S_I$ and $S_Q$ represent the in-phase and out-of-phase baseband channels, respectively; $I_h$ and $Q_h$ represent the $h^{th}$ harmonic extracted from $S_I$ and $S_Q$, respectively; and $a_h(H_0)$ and $b_h(H_0)$ represent absorption and dispersion lineshapes \cite{101} for the $h^{th}$ harmonic.

In the presence of noise, including phase noise, Eq. (7.1) can be modified to

$$
I_h(H_0) = a_h(H_0) \cos \phi_0 - (b_h(H_0) + p) \sin \phi_0 + u
Q_h(H_0) = a_h(H_0) \sin \phi_0 + (b_h(H_0) + p) \cos \phi_0 + v
$$

(7.2)
where \( p \) represents phase noise and has uncorrelated zero-mean Gaussian entries with variance \( \sigma_p^2 \). The sampled noise values in \( u \) and \( v \) represent collective noise from all other sources (primarily amplifiers) in the in-phase and out-of-phase channels, respectively. Both \( u \) and \( v \) are independent and identically distributed Gaussian random variables with variance \( \sigma_0^2 \). For \( \phi_0 = 0 \), Fig. 7.4 shows Cramér-Rao lower bound (CRLB) and corresponding simulation results displaying the impact of collecting multiple harmonics on the estimation error of full-width half-maximum (FWHM) linewidth \( \tau \) for varying degrees of phase noise.

The digital receiver considered here provides quadrature detection with respect to the microwave phase but only a single-channel (in-phase) detection with respect to the field modulation phase. Under nonsaturating conditions, the out-of-phase field modulation channel contains negligible energy and hence can be ignored.

### 7.2.4 Parameter Estimation

For the spectroscopic data, the unknown parameters include linewidth \( \tau \), spin density \( d \), microwave phase \( \phi_0 \), baseline offset (one per each harmonic component), baseline slope (one per each harmonic component), center field, and modulation amplitude \( H_m \). For \( \phi_0 \neq 0 \), the absorption \( (a_h) \) and dispersion \( (b_h) \) components get mixed (Eq. 7.2) and so does the phase noise. If \( \sigma_p^2 \) is not negligible compared to \( \sigma_0^2 \), the contamination from phase noise can adversely affect the SNR of both \( I_h \) and \( Q_h \) components. Therefore, in order to best estimate linewidth, it is important to estimate and adjust the nuisance parameter \( \phi_0 \).

In this work, we have adopted a postprocessing approach, termed as iterative phase rotation estimation (IPRE), to compute the unknown parameters by jointly
Fig. 7.4: Simulation (dotted line) and CRLB (solid line) results showing the impact of multiple harmonics with (gray) and without (black) the phase noise. FWHM linewidth $\tau = 1$ G and field modulation amplitude $H_m = 1$ G (a) and $H_m = 3$ G (b). For each parameter set, 500 trial runs are considered for the simulation.
processing the multiple harmonics. A pseudo code for the IPRE implementation is as follows:

**Initialization**

\[
\begin{align*}
\phi_0^{(0)} &= 0 \\
C_2^{(0)} &= C_2
\end{align*}
\]

**Iteration**

for \( j = 1 : J \)

\[
\begin{align*}
C_2^{(j)} &= \text{ROT}(C_2^{(j-1)}, \phi_0^{(j-1)}) \\
S_I^{(j)} &= C_1 C_2^{(j)} \\
S_Q^{(j)} &= C_1 \tilde{C}_2^{(j)} \\
I_h^{(j)} &= \text{MF}(S_I^{(j)}, h\omega_m) \\
Q_h^{(j)} &= \text{MF}(S_Q^{(j)}, h\omega_m) \\
\{\phi_0^{(j)}, \tau^{(j)}, d^{(j)}\} &= \text{WLS}(I_h^{(j)}, Q_h^{(j)})
\end{align*}
\]

end

where \( \text{ROT}(C_2^{(j-1)}, \phi_0^{(j-1)}) \) represents phase rotation of \( C_2^{(j-1)} \) by \( \phi_0^{(j-1)} \), MF represents digital matched filtering, WLS represents weighted least-squares curve fitting, and \( j \) indicates the iteration number. Note, for \( \phi_0^{(0)} = 0 \), \( C_2^{(1)} = C_2^{(0)} = C_2 \).

In the first iteration of the IPRE, a weighted least-squares curve fitting is performed on the quadrature harmonics, \( I_h^{(1)} \) and \( Q_h^{(1)} \), extracted from the original data \( C_1 \) and \( C_2 \). The estimated microwave phase from iteration 1 is denoted by \( \phi_0^{(1)} \). In the second iteration, \( C_2^{(1)} \) is rotated by \( \phi_0^{(1)} \), and this phase-rotated version of \( C_2 \) is denoted by \( C_2^{(2)} \). Both \( S_I^{(2)} \) and \( S_Q^{(2)} \) are reconstructed by multiplication of \( C_1 \) with
phase-rotated $C_2^{(2)}$ and $\tilde{C}_2^{(2)}$, respectively. To yield individual harmonics, $S_I^{(2)}$ and $S_Q^{(2)}$ are matched filtered with the synthetically generated modulation waveform and its harmonics. The iterative process is repeated until a convergence criterion is reached.

When $\phi_0^{(j)}$ approaches zero, the corresponding $I_h^{(j)}$ and $Q_h^{(j)}$ approximate pure absorption and dispersion lineshapes of the $h^{th}$ harmonic, respectively. In each iteration, the curve fitting is performed using nonlinear weighted least-squares, with weighting of $I_h^{(j)}$ and $Q_h^{(j)}$ proportional to $1/\sqrt{\sigma_0^2 + \sigma_p^2 \sin^2 \phi_0^{(j)}}$ and $1/\sqrt{\sigma_0^2 + \sigma_p^2 \cos^2 \phi_0^{(j)}}$, respectively. Since the true values of $\sigma_0^2$ and $\sigma_p^2$ may not be known, approximate values can be estimated from the tails of the Fourier transform of $I_h^{(j)}$ and $Q_h^{(j)}$. Alternatively, the process of least-squares can be performed twice within each iteration, such that $\hat{\sigma}_0^2$ and $\hat{\sigma}_p^2$ estimated from the residuals of the first unweighted least-squares curve fitting are used in the second weighted least-squares curve fitting.

For the simulation and experimental studies reported in this work, we terminated the IPRE after only two iterations. We observed a very rapid convergence of the IPRE and increasing the number of iterations beyond two did not provide further improvement. For cases where slow convergence is expected, for example in extremely low SNR, it is possible to increase the number of iterations. The parameters estimated by the IPRE are locally convergent to a maximum-likelihood estimate for the signal model in Eq. 7.41. Although it is possible to phase-rotate the reconstructed harmonics $I_h$ and $Q_h$ directly, such a procedure would only further mix the various noise terms and generate a suboptimal solution.
7.3 Results

7.3.1 Simulation

The purpose of this simulation study is to establish the benefit of quadrature detection in comparison to the previously reported single channel detection [116]. For $\sigma_p^2 << \sigma_0^2$, adding the second channel provides approximately 3 dB SNR gain irrespective of the $\phi_0$ value. On the other hand, for phase noise power $\sigma_p^2$ which is comparable to or larger than $\sigma_0^2$, the benefit of adding a second channel lies not in an explicit 3 dB gain in SNR but rather in the ability to accurately estimate $\phi_0$. Even a small $\phi_0$, if unaccounted, can result in a degraded estimation of $\tau$. Figure 7.5 compares the performance of a quadrature receiver with that of a single-channel receiver, for varying values of $\phi_0$. For a single-channel receiver, a complex Lorentzian signal model [148] was used to estimate $\tau$, while for a quadrature receiver the proposed IPRE was used for the estimation.

7.3.2 L-band Spectroscopy

A spectroscopy experiment was conducted on an L-band system equipped with the proposed digital receiver. The related parameters of the system are reported in Table 7.1 and 7.2. The sample was made from a single small crystal of LiNc-BuO [149] sealed in a capillary tube under anoxic conditions. A previously measured anoxic $\tau$ was observed to be 0.658 G.

A total of two datasets were collected with nominal field modulation values of 0.25 G and 2.0 G, respectively. After two iterations of IPRE, the actual field modulation values were found to be 0.27 G and 2.08 G, respectively. Each dataset was comprised of 12 repeated identical scans. The scan time was 3.9 s with a sweep width
Fig. 7.5: Impact of collecting two channels for $\sigma^2_p = 0$ (a) and for $\sigma^2_p = 20\sigma^2_0$ (b). First six harmonics are considered for $\tau = 1$ G and $\bar{H}_m = 1$ G for both single-channel and quadrature estimations. Five hundred trial runs are considered for every one degree increment in $\phi_0$. 

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Fig. 7.6: In-phase ($I_h$) and out-of-phase ($Q_h$) harmonics before (a) and after (b) the second iteration of IPRE. From left to right, four harmonics are shown for $H_m = 2.08$ G. The data were collected on an L-band CW spectrometer equipped with the proposed digital receiver. The dashed-line indicates x-axis.

of 10 G. Figure 7.6 shows the effect of microwave phase-rotation on $I_h$ and $Q_h$ harmonics. Figure 7.7 shows the fitting results from iteration 2 of the IPRE. Figure 7.8 displays the noise correlation between $I_h^{(1)}$ and $Q_h^{(1)}$ and also between $I_h^{(2)}$ and $Q_h^{(2)}$. Figure 7.9 compares the standard deviation of estimated $\tau$ based on first harmonic with the estimation based on the first four harmonics.

7.4 Discussion

The phase noise, originating from the microwave source, does not affect the absorption and dispersion equally. The frequency fluctuations due to phase noise enter
Fig. 7.7: The fitted curves $\tilde{I}_h^{(2)}$ and $\tilde{Q}_h^{(2)}$ and the two times magnified residuals corresponding to Fig. 7.6b.

Fig. 7.8: Impact of $C_2$ phase-rotation on the correlation of noise across $I_h$ and $Q_h$. Noise cross-correlation between $I_1^{(1)}$ and $Q_1^{(1)}$ (a) and between $I_1^{(2)}$ and $Q_1^{(2)}$ (b) computed from the residuals shown in the Fig.
Fig. 7.9: Impact of collecting multiple harmonics on standard error of \( \tau \) estimation. The experiment was conducted on a L-band CW EPR system equipped with the proposed quadrature digital receiver. Twelve scans were collected for each modulation amplitude.

as a first-order effect for the dispersion and a second-order effect for the absorption [150]. Therefore, when present in moderation, the phase noise manifests itself almost exclusively in the dispersion. The noise from the other sources, such as the noise from the LNA and the thermal noise from the resonator, however, tends to affect both absorption and dispersion equally. Therefore, for the noise model considered (Eq. 7.2), \( I_h \) and \( Q_h \) components have equal and independent noise terms, \( u \) and \( v \) respectively, as well as a shared noise term, \( p \), arising from the phase noise.

The relocation of phase-noise exclusively to the out-of-phase channel requires adjusting unknown \( \phi_0 \) to zero. The digital detection, with its retrospective digital data processing capabilities, allows for an accurate estimation and compensation of \( \phi_0 \), eliminating the requirement of manual tuning or additional hardware development. The proposed IPRE relocates the phase noise entirely to the out-of-phase channel.
by iteratively estimating $\phi_0$ and phase-rotating $C_2$. Figure 7.5 compares, for the simulated data, the performance of a quadrature receiver coupled with the IPRE to that of a signal-channel receiver. Figure 7.5a suggests an approximately 3 dB gain in SNR for adding the second channel when the phase noise is negligible. For cases with considerable phase noise, Fig. 7.5b shows a microwave phase-independent performance of the IPRE as compared to a single channel detection whose performance heavily relies on the $\phi_0$ value. Different selections of $\tau$ and $H_m$ yielded similar trends. For the simulation, we chose $\sigma_p^2 = 20\sigma_0^2$ because in the preliminary testing of our digital receiver we consistently encountered $\sigma_p^2$ values which were 10 to 20 times $\sigma_0^2$ depending on the microwave power level.

Figure 7.6 displays one of the measured datasets before and after the second iteration of IPRE, highlighting the transfer of the phase noise from the in-phase to the out-of-phase channel. For the dataset shown in Fig. 7.6, the noise variances were $5.06 \times 10^{-4}$ and $8.95 \times 10^{-4}$ in $I_1^{(1)}$ and $Q_1^{(1)}$, respectively, and $1.60 \times 10^{-4}$ and $12.2 \times 10^{-4}$ in $I_1^{(2)}$ and $Q_1^{(2)}$, respectively. Fig. 7.8 displays the noise correlation, computed from residuals of the curve fitting, after the first and second iterations of the IPRE. A considerable decrease in the correlation is a direct consequence of $\phi_0^{(2)} \rightarrow 0$. The noise correlation, which gets smaller with each iteration of the IPRE, is ignored in the estimation process, but can be readily incorporated to provide an estimation under a correlated Gaussian noise model.

Figure 7.9 illustrates the benefit of collecting multiple harmonics. The standard error of estimation based on the first four harmonics is 29% lower than that of first harmonic alone collected at 2.08 G field modulation, which translates to approximately 50% reduction in the acquisition time. Further speed up is possible by considering

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more harmonics and by optimizing the field modulation amplitude. As expected, adding more harmonics for small $H_m$ does not improve the estimation of $\tau$ while for high $H_m$ the estimation of $\tau$ progressively improves by using more harmonics. For the experimental data, the estimated value of $\phi_0^{(2)}$ in degrees was $0.026 \pm 0.38$.

All the postprocessing was performed in Matlab (Mathorks, MA) on a computer equipped with 2.66 GHz dual core Intel CPU, 8 GB RAM, and 64-bit CentOS operating system. The sampled data, $C_1$ and $C_2$, from each scan were decomposed into 1024 data blocks with each block corresponding to 38 ms of scan time. A decomposition into 4096 blocks (data not shown) produced similar results. The reconstruction of four absorption and four dispersion harmonics, which involved two iterations of the IPRE, took nearly 35 mins. Because the computationally expensive processing is conducted block-by-block, parallelization of the implementation is trivial. Likewise, use of field programmable gate array can accelerate the processing. In the presence of the AFC and field modulation, the instantaneous frequency of $C_2$ continuously varied along the scan, making the synthesis of a potentially cleaner digital version of $C_2$ difficult. We observed that using experimentally observed $C_2$ instead of a digitally estimated replica tone produced better results.

The baseline drift, possibly due to microphonics, was more prominent in the first harmonic. The problem was handled by introducing additional unknowns, one for the offset and one for the slope, for each harmonic component. Also, the nuisance parameters of field modulation amplitude and center field were likewise jointly estimated with the parameters of interest, i.e., linewidth and spin density.
7.5 Conclusions

A quadrature digital receiver and associated signal estimation procedure are reported for L-band EPR spectroscopy. The data acquisition and processing of multiple harmonics in both in-phase and out-of-phase channels are presented. The receiver allows direct digital down conversion, with heterodyne processing using digital capture of the microwave reference signal. Thus, the receiver avoids noise and nonlinearity associated with analog mixers. The retrospective signal processing is suitable for arbitrary microwave phase and arbitrary levels of oscillator phase noise. Simulation and experimental data illustrate the application and relative merits of our design. For the settings shown, the receiver provided 50% reduction in acquisition time when comparing results from first four harmonics to those of first harmonic alone. Even higher accelerations, under different parameter settings, are possible.
CHAPTER 8

FUTURE DIRECTIONS

This thesis considers problems in sparse reconstruction and electronic parametric resonance imaging. There are many open and interesting problems remaining in these two areas. Some future research directions most relevant to the work presented in this thesis are given below.

8.1 Bound Analysis with Random Matrices

In Chapter 4 the results are based on restricted isometry property which is a sufficient condition for stable recovery of sparse signals. This condition typically leads to much weaker bounds than what we observe from numerical experiments. There are many interesting results in the literature for deterministic signal model where it is assumed that the entries of the measurement matrix are drawn randomly from Gaussian or Bernoulli distribution. These results are typically tighter than the results obtained assuming RIP. In many scenarios, it is also possible to obtain necessary conditions with this assumption. It will be interesting to do a similar analysis for the Bernoulli-Gaussian signal model with measurement matrices having random i.i.d. entries.
8.2 Joint Processing of Spectra for Spectral-Spatial Imaging

In Chapters 5 and 6 we developed a forward model for EPR spectral-spatial imaging assuming that only the first harmonic absorption spectrum is available. In Chapter 7 we proposed a digital detection scheme for simultaneous acquisition of multiple harmonics of both absorption and dispersion spectra. The closed form derivation of the forward model becomes extremely complicated when these additional harmonics are considered. Therefore a challenging open problem is to come up with a numerical technique to compute the forward model and jointly process these additional harmonics to improve estimation performance in multi-site EPR oximetry.

8.3 Support Structure

There are many practical problems where the signal is not only sparse but it also has additional structure in its support. For example, in the EPR oximetry application the implanted probe material is *clustered* in space. Natural images are not only sparse in the wavelet domain, but also exhibit *persistence across scales* [151], which makes certain support patterns much more likely. Likewise, in radar images, spatial pixel supports show clustering perpendicular to the look direction [152]. If this support structure is properly exploited then we can further reduce the data requirement for reliable recovery of sparse signals [153]. Support structure has been previously exploited by algorithms proposed in [154, 155, 156, 157]. In [154] it shown by numerical experiments that this reduction in data requirement for same quality of reconstruction can be seen from shifting of phase transition curves. An interesting problem is to analyze how this shifting of phase transition curves depends on the prior knowledge on support structure.
BIBLIOGRAPHY


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