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Impedance-optical Dual-modal Imaging for Tissue Engineering

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THE UNIVERSITY
of EDINBURGH

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Doctor of Philosophy
THE UNIVERSITY OF EDINBURGH

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Biomedical imaging aims to visualize internal structures or functions of the human body, tissues, or cells. Different imaging modalities estimate various parameters and properties, thereby revealing different aspects of the organism's status. Among existing biomedical imaging modalities, such as Electrical Impedance Tomography (EIT), Positron Emission Tomography (PET), and Optical Coherence Tomography (OCT), EIT has demonstrated its unique advantages in non-destructive, non-radioactive imaging, making it suitable for in vivo imaging. After stimulating with small electric currents and recording the voltage between electrodes, EIT reconstructs the conductivity distribution of the region of interest. EIT images can serve as evidence for clinical or medical analysis and diagnosis, as different tissues or distinct physiological states are characterized by different conductivity. For instance, EIT has been applied to lung function monitoring, breast cancer screening, and 3D cell culture monitoring. However, EIT suffers from low image quality concerning structure preservation, background artifact suppression, and differentiation of conductivity contrasts, preventing it from quantitative analysis and limiting its further applications in biomedical fields. Therefore, this thesis aims to address the low quality of the EIT images by using the EIT-optical multi-modal imaging approach.

The first attempt to incorporate information from optical imaging into EIT image reconstruction is conducted using non-overlapping group sparsity regularization. The proposed algorithm consists of three steps. The first step involves segmenting the optical image to acquire its binary counterpart. Then, grouping is done based on the segmented image. Finally, the EIT image reconstruction problem is formulated as a penalized optimization problem and solved using the alternating direction method of multipliers (ADMM). The algorithm is evaluated in simulations and real-world experiments, both of which demonstrate that IGGS can generate more accurate contrasts of conductivity distribution than comparative algorithms. This suggests the potential for performing impedance-based quantitative analysis in tissue engineering.

The aforementioned algorithm needs to segment optical images, which introduces additional computational costs. Furthermore, the formulation of grouping rules relies on experience or observation, which may deviate from objective facts. Therefore, another multi-modal image reconstruction algorithm is proposed by utilizing the kernel approach. The kernel-based algorithm is segmentation-free and incorporates information from optical imaging into EIT reconstruction through the kernel matrix. The construction of the kernel matrix is based on the
characteristics of the optical image and does not involve human-made rules. Therefore, the kernel-based algorithm overcomes part of the limitations of the aforementioned algorithm and it is evaluated through numerical simulations and real experiments, with the results indicating the effectiveness of the kernel-based method.

The two previous algorithms have specific limitations. The first one requires additional image segmentation, while the latter one exhibits unsatisfactory artifact suppression capabilities. To address these limitations, a new algorithm based on Overlapping Group Lasso and Laplacian (OGLL) regularization is further proposed. The OGLL algorithm groups conductivity changes based on the local characteristics of the auxiliary image, integrating structural information with the overlapping group lasso. This approach eliminates the need for finely crafted grouping rules. Since group sparsity promotes group-wise sparsity, OGLL possesses strong noise resistance capabilities. Consequently, OGLL enhances structure preservation, background artifact suppression, and conductivity contrast differentiation compared to existing algorithms. The results of OGLL demonstrate that a multi-modal approach can achieve superior image quality compared to single-modal methods.

Considering the superior performance of deep learning in nonlinear fitting and latent feature expression, the exploration of deep learning in multi-modal EIT image reconstruction is an appealing prospect. Consequently, in this thesis, we propose a learning-based multi-modal imaging framework for 3D cell culture imaging. This framework consists of three components: an impedance-optical dual-modal sensor, a guidance image processing algorithm, and a deep learning model called the Multi-Scale Feature Cross Fusion Network (MSFCF-Net) for information fusion. We evaluate the performance of this dual-modal framework through numerical simulations and MCF-7 cell imaging experiments. The results demonstrate a notable improvement in image quality using the proposed method, highlighting the potential of impedance-optical joint imaging to simultaneously reveal structural and functional information at the tissue level.

In summary, this thesis fills a research gap in tissue imaging by combining EIT and optical imaging. The results obtained in this study validate the effectiveness and enhancement of bioimpedance estimation through the proposed multi-modal imaging approach. Furthermore, these results suggest that the multi-modal imaging approach has the potential to catalyze breakthroughs in tissue engineering.
Biomedical imaging plays a crucial role in revealing the inner workings of the human body, tissues, and cells. Various imaging techniques are used to capture diverse aspects of an organism’s condition. Among these methods, Electrical Impedance Tomography (EIT) stands out for its non-destructive, non-radioactive nature, making it ideal for in vivo applications. EIT operates by applying small electric currents to a region of interest and recording the resulting voltage between electrodes. This process allows EIT to reconstruct the region’s conductivity distribution. EIT images are valuable in clinical and medical settings because they can distinguish between different tissues and physiological states based on unique conductivity patterns. However, EIT faces challenges related to image quality, including issues with structure preservation, background artifact suppression, and differentiation of conductivity contrasts. These limitations hinder its use in quantitative analysis and further restrict its potential applications in the field of biomedical imaging. Consequently, this thesis is dedicated to improving the quality of EIT images through the innovative EIT-optical multi-modal imaging approach.

To address this, the thesis introduces an EIT-optical multi-modal imaging approach. Centered at the multi-modal imaging framework, one algorithm combines optical information with EIT using a group sparsity regularization algorithm, demonstrating enhanced accuracy in conductivity distribution contrasts. The second algorithm employs a kernel-based approach, eliminating image segmentation and human-made grouping rules. This method overcomes some limitations but has room for improvement in artifact suppression. To further enhance EIT image quality, a novel algorithm based on Overlapping Group Lasso and Laplacian (OGLL) regularization is proposed. OGLL utilizes local characteristics from an auxiliary image, improving structure preservation, artifact suppression, and conductivity contrast differentiation. Results show that OGLL outperforms existing algorithms.

Additionally, the thesis explores the potential of deep learning in multi-modal EIT image reconstruction by introducing a framework that combines impedance-optical dual-modal sensors with a deep learning model known as the Multi-Scale Feature Cross Fusion Network (MSFCF-Net). This approach substantially enhances image quality, offering the promise of simultaneously providing insights into both the structural and functional aspects of tissue imaging.

All of the methods presented in the thesis undergo comprehensive evaluation through simulations and real experiments. The results unequivocally demonstrate the effectiveness of the multi-modal approach in the context of tissue engineering. These findings underscore the immense potential of amalgamating multiple imaging modalities to achieve a comprehensive analysis of tissue structures and functions.
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I want to begin by extending my heartfelt appreciation to my principal supervisor, Dr. Yunjie Yang. His unwavering support and the opportunity to engage in this captivating project have been invaluable to me. I am deeply grateful for his guidance and encouragement, which have not only influenced my academic pursuits but also enriched my daily life. Without his patience, assistance, and insightful suggestions, none of my accomplishments would have been attainable.

I also wish to express my gratitude to my assistant advisors, Dr. Pierre Bagnaninchi and Dr. Michael Chen, for their valuable suggestions and technical assistance during my doctoral studies. Their guidance has been instrumental in shaping my research and ensuring its success.

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Declaration

I declare that this thesis was composed by myself, that the work contained herein is my own except where explicitly stated otherwise in the text, and that this work has not been submitted for any other degree or professional qualification except as specified.

Zhe Liu
8th January 2024
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<td>Two Dimensional</td>
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<td>3D</td>
<td>Three Dimensional</td>
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<td>ADMM</td>
<td>Alternating Direction Method of Multipliers</td>
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<td>CEM</td>
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Chapter 1

Introduction

1.1 Background and Motivation

The significance of 3D cell culture extends widely, as it offers a superior mimicry of living tissues compared to cell monolayers, thereby profoundly impacting drug screening (Cukierman, Pankov, Stevens, & Yamada, 2001; Pampaloni, Reynaud, & Stelzer, 2007). Enhanced models of cellular behaviors hold the potential to advance research and treatment of human diseases while minimizing reliance on animal testing. Current techniques, such as Transmission Electron Microscopy (TEM) (Graham & Orenstein, 2007), confocal microscopy (Martínez-Santibañez, Cho, & Lumeng, 2014), and micro CT (Tuan & Hutmacher, 2005), etc. have greatly improved our understanding of tissue engineering and cell-material interactions. However, these methods involve tissue fixation, cutting, and staining, making samples unsuitable for further studies. MTT and MTS assays offer an alternative to assess cell viability in biomaterials, but they are time-consuming and require dyeing (Marlina, Shu, AbuBakar, & Zandi, 2015). Regrettably, these assays cannot provide a real-time, non-destructive, and label-free assessment of cellular functions, e.g. growth, proliferation, differentiation, and viability. Consequently, a key challenge in 3D cell culture lies in obtaining comprehensive insights into cellular states over time. As a result, there is a search for an appropriate imaging technique to enable continuous and non-destructive monitoring of 3D cell culture.

Electrical Impedance Tomography (EIT) emerges as a tomographic imaging method capable of revealing conductivity distribution within a domain’s interior by injecting boundary currents and measuring induced voltages (Brown, 2003; Metherall, Barber, Smallwood, & Brown, 1996). EIT has demonstrated its unique advantages in non-destructive, non-radioactive imaging, making it suitable for in vivo imaging. Consequently, EIT images can serve as evidence for clinical or medical analysis and diagnosis, as different tissues or distinct physiological states are characterized by different conductivity (Adler & Boyle, 2017; Miklavčič, Pavšelj, & Hart, 2006). For instance, EIT has been applied to lung function monitoring (Frerichs et al., 2002; K. Zhang et al., 2020), nerve imaging (Aristovich et al., 2018; Ravagli et al., 2020), and gastric functional monitoring (Darima, Kawashima, & Takei, 2022). Especially, in tissue engineering, it has been demonstrated that cellular electrical parameters can offer insight into cell viability (R. Pethig & Kell, 1987). Recent advancements have introduced miniaturized EIT
for imaging the conductivity distribution of 3D cultured cells in both static and dynamic settings (Wu, Yang, Bagnaninchi, & Jia, 2018; Y. Yang et al., 2016; Y. Yang, Wu, Jia, & Bagnaninchi, 2019; Yin, Wu, Jia, & Yang, 2018). Nevertheless, the less-than-optimal image quality of EIT stands as a critical limiting factor when endeavoring to quantitatively analyze the intricate properties and behaviors exhibited by 3D cultured cells in the realm of tissue engineering applications.

Previous efforts aimed at enhancing the image quality of EIT have primarily concentrated on refining image reconstruction algorithms. In this context, predominant model-based methods mostly revolve around regularization, which involves incorporating prior knowledge into the image reconstruction process. Prominent state-of-the-art regularization techniques for EIT include $l_1$ regularization (Tehrani, McEwan, Jin, & Van Schaik, 2012; Q. Wang et al., 2012), Total Variation (TV) regularization (Gong et al., 2018; Jung & Yun, 2014), and Adaptive Group Sparsity (AGS) regularization (Y. Yang & Jia, 2017a; Y. Yang, Wu, & Jia, 2017), among others. These algorithms have proven effective in obtaining high image quality but at the expense of computational efficiency or intricate parameter tuning. Deep learning (DL) has recently demonstrated its potential in solving the nonlinear EIT inverse problem. Several end-to-end deep learning-based approaches have been documented for achieving high-quality EIT image reconstruction (Hu, Lu, & Yang, 2019; F. Li, Tan, & Dong, 2020; Tan, Lv, Dong, & Takei, 2018). However, the efficacy of these methods heavily relies on the quantity and quality of the training dataset. An alternative approach involves amalgamating model-based methods with deep learning to leverage the strengths of both paradigms. Previous research includes utilizing deep learning to facilitate model error compensation (Smyl, Tallman, Black, Hauptmann, & Liu, 2021) or enhance the performance of model-based methods (Chen, Xiang, Bagnaninchi, & Yang, 2022). Nevertheless, the attainment of precise structural information in tandem with EIT imaging using a ‘single-modal’ sensor, such as EIT alone, continues to pose challenges.

More recently, endeavors have been focused on dual-modal or multi-modal approaches to complement EIT. For example, Hao et al. (H. Liu, Zhao, Tan, & Dong, 2019) introduced an EIT and ultrasound dual-modality method where ultrasound sensing data is utilized as prior information to enhance boundary preservation in EIT reconstructions. In a similar vein, Li et al. integrated X-ray tomography as an auxiliary imaging modality. The structural information derived from X-ray imaging is seamlessly incorporated into EIT inversion using the cross-gradient method (Z. Li, Zhang, Liu, & Du, 2019). These studies have demonstrated the potential of multi-modal imaging in combining complementary information and enhancing the quality of EIT images.
1.1. Background and Motivation

Despite these promising advancements, the application of multi-modal imaging techniques in the realm of tissue engineering remains relatively unexplored. Integrating multi-modal information has the potential to revolutionize our understanding of 3D cell cultures, enabling a more comprehensive analysis of their behavior and properties. By leveraging the strengths of different imaging modalities, researchers can pave the way for more accurate and insightful investigations into the intricate world of 3D cell culturing within tissue engineering applications.

1.2. Aims and Objectives

Inspired by multi-modal imaging, and in order to tackle the spatial resolution issues of EIT for tissue engineering applications, the aim of this research is to develop an innovative bioimpedance-optical, dual-modal imaging platform for 3D cell culturing imaging. It includes designing miniature optical and bioimpedance dual-modal sensors, investigating robust image reconstruction and fusion algorithms, and testing and benchmarking the platform. To fulfill the aim, the following objectives have been set:

1. Develop the miniature bioimpedance-optical, dual-modal sensors for tissue imaging. The goal is to achieve effective and robust multi-signal sensing, i.e. optical and electrical signals.
2. Develop advanced image reconstruction and fusion algorithms based on physical models or machine learning corresponding to manufactured sensors. This will focus on reconstructing high-quality, biologically meaningful images from multiple tomography modalities.
3. Perform real-world experimental validation. The developed techniques will be thoroughly tested and validated on tissue phantoms, 3D cultivated cells, and real biological tissues.

1.3. Main Contributions

The main contributions of this thesis are summarized below:

1. The thesis proposed a general EIT-optical dual-modal imaging framework for tissue engineering (see Fig 1.1). Any suitable optical sensor can be seamlessly integrated into this dual-modal system, provided that it can offer precise structural information. This framework serves as the basis for the subsequent algorithm development, encompassing both model-based and learning-based approaches.
2. Three model-based multi-modal algorithms were developed for EIT, namely Image-Guided Group Sparsity (IGGS), Kernel Method, and Overlapping Group Lasso and Laplacian (OGLL) regularization (see Fig. 1.2). Among these, IGGS and the Kernel Method are segmentation-based and segmentation-free algorithms, respectively. OGLL
1.3. Main Contributions

Dual-Modal Sensor

**Figure 1.1:** The schematic diagram illustrates the proposed general EIT-optical imaging framework. Please note that the sensor depicted in this figure is for conceptual purposes only and does not represent an actual sensor.

is a more advanced algorithm that integrates the strengths of the preceding two methods. The effectiveness of these algorithms was verified by simulation and real experiments. The results demonstrated that the performance of the multi-modal algorithms is superior to that of the single-modal algorithms.

3. In the context of learning-based multi-modal imaging, this thesis introduced a special dual-modal imaging framework. This framework employs an innovative approach to indirect information fusion, specifically designed to tackle the hurdle of directly employing optical images for training deep learning models. This approach holds the potential for extension to other imaging scenarios involving learning-based multi-modal image reconstruction that encounters analogous challenges. In addition, the proposed neural network named multi-scale feature cross fusion network (MSFCF-Net, see Fig. 1.2) is verified effective in simulation data reconstruction and MCF-7 cell aggregates imaging.

4. The evidence presented through the outcomes of the methods developed in this thesis substantiates that the multi-modal imaging approach significantly enhances EIT image quality in comparison to single-modal techniques. Specifically, the developed multi-modal algorithms showcased superior performance in terms of structural preservation, suppression of background artifacts, and differentiation of conductivity levels.
1.3. Main Contributions

The developed algorithms are categorized and interrelated as follows: IGGS and the Kernel Method fall into distinct algorithmic categories, specifically segmentation-based and segmentation-free approaches. OGLL integrates the strengths of both IGGS and the Kernel Method, and it is also a segmentation-free method. These three algorithms belong to model-based algorithms. The central algorithm for learning-based multi-modal imaging is MSFCF-Net, which is an end-to-end neural network.

These contributions play a pivotal role in advancing bioimpedance tomography as a potent non-destructive and real-time imaging modality for tissue engineering. The pertinent results have been published in or submitted to esteemed journals and international conferences, as outlined in the publication list.

1.4 Overview of the Thesis

The thesis encompasses seven chapters. Aside from the introduction, the remainder is organized as follows:

Chapter 2 provides a brief review of the principles of EIT, the EIT-incorporated multi-modal systems, state-of-the-art single-modal and multi-modal EIT image reconstruction algorithms, and the applications and challenges of EIT in tissue engineering.

Chapter 3 integrates optical imaging into EIT to enhance image quality and introduces a segmentation-based dual-modal reconstruction algorithm called Image-Guided Group Sparsity (IGGS). This algorithm combines RGB microscopic images and EIT measurements to extract conductivity distribution features, resulting in improved image quality. Numerical simulations and real-world experiments confirm IGGS’s effectiveness. When compared to given algorithms, IGGS outperforms them in shape preservation, background artifact reduction, and conductivity contrast differentiation.
1.4. Overview of the Thesis

Chapter 4 develops a segmentation-free multi-modal EIT image reconstruction method as an alternative to IGGS, using a kernel approach to fuse information and incorporate structural prior from high-res auxiliary images into the EIT inversion via the kernel matrix. This adaptable technique can improve EIT images, outperforming comparison methods in simulations and experiments while also suppressing the interference of imaging-irrelevant objects in the auxiliary image.

Chapter 5 proposes another segmentation-free multi-modal EIT image reconstruction algorithm named Overlapping Group Lasso and Laplacian (OGLL) regularization, which combines the advantages of the IGGS and Kernel Method. The OGLL incorporates the structural prior through overlapping group lasso and the grouping rules are inspired by the Kernel Method. The group-wise sparsity gives the OGLL a satisfactory capability of suppressing background artifacts with no need to segment the auxiliary image. Surprisingly, this mixed regularization method also demonstrated a more accurate recovery of the conductivity levels among the given algorithms.

Chapter 6 introduces an impedance-optical dual-modal imaging framework aimed at enhancing image quality for 3D cell culture imaging. The framework incorporates an impedance-optical dual-modal sensor, a guidance image processing algorithm, and a deep learning model named multi-scale feature cross fusion network (MSFCF-Net) for fusing information. Numerical simulations and cell imaging experiments demonstrate notable image quality improvement, showcasing the potential of impedance-optical joint imaging to simultaneously reveal structural and functional details of tissue-level targets.

Finally, Chapter 7 offers a summary of the thesis’s scientific contributions and explores potential avenues for future research.
Chapter 2

Literature Review

2.1 Introduction

This chapter begins with a concise introduction to the principle of EIT, encompassing both the forward and the inverse problems. Subsequently, various EIT-incorporated multi-modal imaging systems are described. Building upon the single-modal and multi-modal imaging systems, corresponding state-of-the-art EIT image reconstruction algorithms are summarized. Finally, the chapter delves into the emerging applications of EIT in tissue engineering, providing a comprehensive review of its uses. Additionally, the limitations and challenges associated with these applications are discussed.

2.2 Principle of Electrical Impedance Tomography

EIT consists of two sub-problems, i.e. the forward and inverse problems. Given a known conductivity distribution, the forward problem of EIT calculates the electrical potential distribution within the sensing region. The boundary voltage measurements can also be gained by solving the EIT forward problem. The inverse problem of EIT estimates the discrete conductivity distribution of the sensing region based on voltage measurements through the reconstruction algorithm.

2.2.1 Forward Problem

Consider an imaging region $\mathcal{U} \subset \mathbb{R}^D$, $D = 2$ or $3$, $E$ electrodes represented by $\{e_i\}_{i=1}^E$ are evenly attached on its boundary $\partial \mathcal{U}$. Assuming $\sigma(p) \in \mathbb{R}$, $p \in \mathcal{U}$, denotes the continuous-space real-valued conductivity, the commonly-used Complete Electrode Model (CEM) is formulated as (Somersalo, Cheney, & Isaacson, 1992):

$$\nabla \cdot [\sigma(p) \nabla u(p)] = 0, \quad p \in \mathcal{U} \quad (2.1)$$

$$u(p) + z_i \sigma(p) \frac{\partial u(p)}{\partial n} = U_i, \quad p \in e_i, \quad i = 1, 2, \ldots, E \quad (2.2)$$
2.2. Principle of Electrical Impedance Tomography

Figure 2.1: Sixteen-electrode circular 2D EIT sensor with two inclusions inside. In the imaging region $\Omega$, the red color indicates higher electric potential, and the blue color represents lower electric potential.

\[
\int_{e_i} \sigma(p) \frac{\partial u(p)}{\partial n} dp = I_i, \quad i = 1, 2, \ldots, E
\]  
(2.3)

\[
\sigma(p) \frac{\partial u(p)}{\partial n} = 0, \quad p \in \partial \Omega \setminus \bigcup_{i=1}^{E} e_i
\]  
(2.4)

\[
\sum_{i=1}^{E} I_i = 0, \quad \sum_{i=1}^{E} U_i = 0
\]  
(2.5)

where $u(p)$ denotes the electrical potential in the sensing region and $\hat{n}$ represents the outer unit normal of $\partial \Omega$. $z_i$, $U_i$ and $I_i$ are the contact impedance, electrical potential, and the injected current on $e_i$, respectively. Equation (2.5) guarantees the existence and uniqueness of the solution of (2.1).

Since obtaining an analytical solution for the above boundary-value problem is challenging, the Finite Element Method (FEM) is commonly employed to calculate the numerical solution (G. Xu et al., 2005). In FEM, a dense triangular mesh is used to represent the discrete conductivity distribution. In each triangular simplex, the conductivity distribution is considered homogeneous. Subsequently, the electric potentials of the vertices of these triangular simplices are approximated by solving a linear system. Finally, the continuous electrical potential distribution can be estimated from these discrete solutions by the interpolation algorithm. A 2D example of the EIT sensing principles with the induced electric potential distribution is illustrated in Fig. 2.1.
2.2. Principle of Electrical Impedance Tomography

split the imaging domain using horizontal and vertical lines.

The value in a grid is treated as a constant. If the center point of a grid is in the imaging region, that grid represents an EIT image pixel. Therefore, we can use a finite number of digits to represent the \( \sigma_x, \sigma_y \). In the inverse problem, these digits are unknown. We will assemble them into a column list of numbers based on the predefined orders, forming the unknown conductivity vector \( \sigma \in \mathbb{R}^{3228} \).

Figure 2.2: The process of the discretization of \( \sigma(p) \) in 2D case, where \( p = (x, y) \). The pastel pink circular area represents the imaging region. In this example, the square mesh is adopted, and \( N = 3228 \).

2.2.2 Inverse Problem

In EIT, the inverse problem begins with the partition of the imaging region, namely, the construction of the inverse mesh. The inverse mesh should be much more coarser than the forward mesh. Suppose we divided the imaging region into \( N \) disjoint subregions satisfying 
\[ \Omega = \bigcup_{n=1}^{N} \Omega_n \] and the conductivity in a subregion is considered as a constant. An example of \( \sigma(p) \) discretization is illustrated in Fig. 2.2. It can be readily expressed that the nonlinear relationship between the discrete conductivity distribution \( \sigma \in \mathbb{R}^N \) and the complete EIT measurements \( V \in \mathbb{R}^M \) (Seo & Woo, 2012):

\[
V = F(\sigma),
\]  

(2.6)
where \( F \) represents the known mapping named the nonlinear forward model. Thus, the EIT inverse problem can be formulated as:

\[
\min_{\sigma} \frac{1}{2} ||F(\sigma) - V||^2 + \bar{\eta} \tilde{R}(\sigma), \tag{2.7}
\]

where \( || \cdot || \) denotes the \( l_2 \) norm, \( \tilde{R} : \mathbb{R}^N \rightarrow \mathbb{R} \) represents the regularization function, which encodes the prior information and \( \bar{\eta} > 0 \) accounts for the regularization parameter. Because of the time consuming of solving (2.7), the EIT inverse problem is commonly based on the linear forward model (Brandstatter, 2003; Polydorides & Lionheart, 2002), which is:

\[
\Delta V = J \Delta \sigma, \tag{2.8}
\]

where \( \Delta V = V_o - V_r \) and \( \Delta \sigma = \sigma_o - \sigma_r \). The subscripts of 'o' and 'r' represent the corresponding quantities at the observation and reference time points. \( J \in \mathbb{R}^{M \times N} \) stands for the sensitivity matrix or Jacobian matrix, which is readily expressed as:

\[
J = \frac{\partial V}{\partial \sigma}. \tag{2.9}
\]

Consequently, the EIT inverse problem can also be formulated as:

\[
\min_{\Delta \sigma} \frac{1}{2} ||J \Delta \sigma - \Delta V||^2 + \eta R(\Delta \sigma), \tag{2.10}
\]

where \( R : \mathbb{R}^N \rightarrow \mathbb{R} \) accounts for the regularization function and \( \eta > 0 \) denotes the regularization parameter.

### 2.3 EIT-Incorporated Multi-Modal Imaging Systems

Due to the issue of low spatial resolution in EIT images, several multi-modal imaging approaches have been proposed to improve the EIT image quality (see Fig. 2.3). Among these methods, EIT is combined with at least one other imaging modality to estimate the conductivity distribution map more effectively.

As early as the 1990s, researchers proposed Magnetic Resonance Electrical Impedance Tomography (MREIT) to improve the invertibility of the EIT (Seo & Woo, 2011). The schematic of the MREIT configuration is shown in Fig. 2.3 (a). The process of MREIT imaging involves injecting currents into the imaging region and then employing Magnetic Resonance Imaging (MRI) (Z.-P. Liang & Lauterbur, 2000) to measure the resulting magnetic flux density. Finally,
2.3. EIT-Incorporated Multi-Modal Imaging Systems

The MRI data is utilized to reconstruct the distribution of conductivity. By addressing the ill-posedness of EIT inversion, MREIT significantly improves the quality of EIT images. However, it should be noted that MRI equipment is expensive, and the acquisition time for MREIT is lengthy, thereby limiting the widespread application of MREIT.
In 2011, Doga et al proposed a multi-modal system combining the measured data of the EIT, Magnetic Induction Tomography (MIT), and Induced-Current EIT (ICEIT) to reconstruct the EIT images (Gursoy, Mamatjan, Adler, & Scharfetter, 2011). The configuration of their innovative system is depicted in Fig. 2.3 (b). By combining these modalities, they successfully increased the number of independent measurements, leading to improved ill-conditioning of the inverse problem in conductivity recovery. The results demonstrated the effectiveness of their approach in enhancing image reconstruction.

Furthermore, the combination of EIT and ultrasound imaging is also investigated (G. Liang, Ren, & Dong, 2020; G. Liang, Ren, Zhao, & Dong, 2019; Ren, Liang, & Dong, 2020). The typical configuration of the multi-modal imaging platform is illustrated in Fig. 2.3 (c). The EIT is sensitive to near-boundary perturbations while the ultrasound imaging is sensitive to the perturbations in the center area of the imaging region (G. Liang et al., 2019). Therefore, this type of multi-modal system can improve the homogeneity of the sensitivity. Another configuration of the EIT-Ultrasound imaging was also proposed for muscle health assessment (see 2.3 (d)) (Murphy, Skinner, Martucci, Rutkove, & Halter, 2018). Compared with the commonly used Electrical Impedance Spectroscopy (EIS) measurements, their system performs better in differentiating healthy and diseased tissue. Many algorithms are associated with EIT and ultrasound joint imaging. However, the majority of these algorithms primarily center around shape reconstruction, as evidenced by studies such as (G. Liang et al., 2020; Ren et al., 2020). These algorithms are dedicated to reconstructing the boundary of inclusions. While shape reconstruction is undoubtedly important, it is crucial to recognize that in various applications, particularly within the realm of tissue engineering, the internal conductivity distribution holds equal significance. Consequently, this category of algorithms holds lesser relevance to the central theme of this thesis. As a result, we choose not to delve into a comprehensive review of these algorithms in the subsequent section.

In tissue imaging, dealing with tissue thickness poses a significant challenge for many imaging modalities. For instance, the thickness of the tissue prevents the penetration of light in microscope-based imaging. To address this limitation, Polojärvi et al. introduced a novel approach that combines Optical Projection Tomography (OPT) and Electrical Impedance Tomography (EIT) for the retrieval of the tissue conductivity spectrum (Lehti-Polojärvi et al., 2021). 2.3 (e) illustrates their imaging system. The outcomes of their research demonstrated the system’s capability to distinguish between viable and dead tissues as well as identify stem cells.
A recent study integrated the EIT with Electrical Capacitance Tomography (ECT) with the name Capacitively Coupled Electrical Impedance Tomography (CCEIT) (Y. Jiang et al., 2022). This innovative approach aims to achieve high-quality complex conductivity image reconstruction. The outcomes of the study provided compelling evidence for the effectiveness of this novel system. Furthermore, the authors proved the dual-frequency CCEIT with the two optimized frequencies out-performance the single-frequency CCEIT.

In addition to the aforementioned multi-modal systems, there has been significant research on multi-modal EIT image reconstruction algorithms. These advanced algorithms utilize information from other imaging modalities as priors for the EIT image reconstruction process. Importantly, it should be noted that these approaches are distinct from traditional multi-modal systems, as they do not involve direct integration of non-EIT imaging systems with the EIT hardware. Nonetheless, these innovative methods will be reviewed in the next section.

### 2.4 EIT Image Reconstruction Algorithms

EIT image reconstruction can be classified into two main categories: single-modal algorithms and multi-modal algorithms. Single-modal algorithms rely exclusively on EIT data to reconstruct the EIT images. In contrast, multi-modal algorithms reconstruct EIT images by not only utilizing EIT data but also incorporating measurement data from other imaging modalities. Nevertheless, the number of multi-modal algorithms is significantly lower compared with that of the single-modal algorithms.

Each of these algorithm types can be further divided into two sub-categories: model-based algorithms and learning-based algorithms. Model-based algorithms are formulated based on direct results from the physical model of EIT, encompassing the mathematical representation of the underlying physics and electrical properties of the imaging process. On the other hand, learning-based algorithms take a different approach by acquiring the inverse operator from a substantial volume of training data. The following subsections will provide comprehensive reviews of these approaches.

#### 2.4.1 Single-Modal Algorithms

**Model-based Algorithms**

Various single-modal model-based algorithms can be broadly classified into two categories: direct reconstruction and regularization-based reconstruction.

The direct reconstruction methods are based on the mathematical foundation by A. I. Nachman, which enables obtaining the values of the coefficient $\gamma(p)$ of the elliptic equation $\nabla \cdot (\gamma(p) \nabla u(p)) = 0$ non-iteratively (Here, $p$ represents a point in the two-dimensional space) (Nachman, 1996). The basic process of this method involves transforming the nonlinear conductivity
equation into the Schrödinger equation and then utilizing the method of inverse scattering to solve the resulting inverse problem. Subsequently, several direct-reconstruction-based EIT image reconstruction methods have been extensively investigated. Notably, these methods include the d-bar method (Hamilton, Mueller, & Santos, 2018; Knudsen, Lassas, Mueller, & Siltanen, 2007, 2009), Calderon’s method (Bikowski & Mueller, 2007; Boverman, Kao, Isaacson, & Saulnier, 2009; Shin, Ahmad, & Mueller, 2020), and the factorization method (Gebauer & Hyvönen, 2007; Harrach, Seo, & Woo, 2010; Schmitt, 2009), etc. These direct methods offer a straightforward and easily implemented approach to solving the complex nonlinear inverse problem in EIT imaging. However, the direct methods are not comprehensively compared with the regularization methods.

The regularization-based reconstruction is currently the mainstream approach for high-quality image reconstruction, which starts from the modeled fidelity relationship between the measurements and the discrete conductivity distribution, i.e. the equation (2.6) or (2.8). Different algorithms are mainly characterized by regularization strategies, which incorporate prior information about the structure of the solution. Specifically, these priors can help reduce the size of the feasible set of the formulated optimization problem and endow the solution with the properties underlying the priors. There have been proposed various regularization approaches. For instance, the well-known Tikhonov regularization can be expressed by (Vauhkonen, Vadász, Karjalainen, Somersalo, & Kaipio, 1998):

$$\min_{\Delta \sigma} \frac{1}{2} || J \Delta \sigma - \Delta V ||^2 + \frac{\eta}{2} || T \Delta \sigma ||^2,$$  \hspace{1cm} (2.11)

where $T \in \mathbb{R}^{M \times N}$ is a finely designed constant matrix which is the interface for embedding the prior information. Since this is a convex problem, the solution can be readily expressed by:

$$\Delta \sigma^* = (J^T J + \eta T^T T)^{-1} J^T \Delta V.$$  \hspace{1cm} (2.12)

Commonly, we let $T$ equal to the identity matrix $I \in \mathbb{R}^{M \times N}$. In this situation, the regularization will promote the smoothness of the solution meanwhile improving the invertibility of $J^T J$. The Laplacian matrix $L \in \mathbb{R}^{M \times N}$ can also be selected as the Tikhonov matrix to promote the smoothness of the EIT image (Y. Yang, Jia, Polydorides, & McCann, 2014). In addition, various variants of the Tikhonov regularization method are also explored, such as the algorithm based on nonstationary iterated Tikhonov regularization (J. Wang, 2023), and an improved Tikhonov Regularization which is applied to lung cancer monitoring (Sun, Yue, Hao, Cui, & Wang, 2019).

The second example involves the $L_1$ regularization (or sparsity regularization), whose generic expression is (Vidaurre, Bielza, & Larranaga, 2013):

$$\min_{\Delta \sigma} \frac{1}{2} || J \Delta \sigma - \Delta V ||^2 + \eta \sum_{n=1}^{N} | \Delta \sigma_n |.$$  \hspace{1cm} (2.13)
2.4. EIT Image Reconstruction Algorithms

$L_1$ regularization encourages sparse solution, i.e. making most elements of the solution zero. Thus, it is well-suited for situations where the inclusions in the imaging region are very small (Tehrani et al., 2012; Q. Wang et al., 2012). The extension of the $L_1$ regularization, namely, the $L_{\rho}$ regularization ($0 < \rho < 2$) (J. Li, Yue, Ding, Cui, & Wang, 2019), is also investigated to deeply explore the sparsity structure of the solution. The $L_{\rho}$ regularization term is formulated as: $||\Delta\sigma||_{\rho} = \left(\sum_{n=1}^{N} |\Delta\sigma_n|^\rho\right)^{1/\rho}$.

Another widely employed regularization is Total Variation (TV). Like $L_1$ regularization, it is also a global prior. Differently, TV regularization is mainly adopted to promote edge preservation and noise reduction. The TV-based image reconstruction can be formulated by (Jung & Yun, 2014):

$$\min_{\Delta\sigma} \frac{1}{2} ||J\Delta\sigma - \Delta V||^2 + \eta TV(\Delta\sigma), \tag{2.14}$$

where $TV : \mathbb{R}^N \rightarrow \mathbb{R}$ represents the Total Variation mapping. There are a lot of approaches to approximate the $TV(\Delta\sigma)$. For example, the commonly used differentiable isotropic TV term is expressed as (Q. Wang, Wang, et al., 2021):

$$TV(\Delta\sigma) = \sum_{l,j,k} \left\{ \sum_r \left[ (\nabla_r \Delta\sigma)_{l,j,k} \right]^2 + c \right\}^{-\frac{1}{2}}, \tag{2.15}$$

where $c > 0$ is a small constant and $r \in \{h,w,d\}$. Specifically, $\nabla_h \Delta\sigma$, $\nabla_w \Delta\sigma$, and $\nabla_d \Delta\sigma$ represent the gradient components of $\Delta\sigma$ along the height, width, and depth directions, respectively. $l$, $j$ and $k$ represent the voxel indices when $\Delta\sigma$ is reshaped to a 3D image. The expressions of $\nabla_h \Delta\sigma$, $\nabla_w \Delta\sigma$, and $\nabla_d \Delta\sigma$ are:

$$(\nabla_h \Delta\sigma)_{l,j,k} = (\Delta\sigma)_{l+1,j,k} - (\Delta\sigma)_{l,j,k},$$
$$(\nabla_w \Delta\sigma)_{l,j,k} = (\Delta\sigma)_{l,j+1,k} - (\Delta\sigma)_{l,j,k},$$
$$(\nabla_d \Delta\sigma)_{l,j,k} = (\Delta\sigma)_{l,j,k+1} - (\Delta\sigma)_{l,j,k}. \tag{2.16}$$

Numerous alternative approximations of TV regularization have been extensively explored in EIT. These investigations encompass various works, such as the first-order non-differentiable TV regularization (Borsic, Graham, Adler, & Lionheart, 2009; Jung & Yun, 2014), higher-order TV regularization (Gong et al., 2018), and so forth.

The sparsity structure of the solution is additionally explored through the utilization of the concept of group sparsity. This local prior promotes sparsity within groups of pixels/voxels (Huang & Zhang, 2010), rendering it especially suitable for particular scenarios in tissue engineering, such as 3D cell aggregate culture. The formulation of the group-sparsity-based
EIT image reconstruction is (Yang & Jia, 2017a; Yang et al., 2017):

$$
\min_{\Delta \sigma} \sum_{\epsilon=1}^{G} \omega_{\epsilon} \| \Delta \sigma_{g_{\epsilon}} \|
$$

where \( g_{\epsilon} \) represents the \( \epsilon^{th} \) group of \( \Delta \sigma \) based on the predefined grouping rules and \( \omega_{\epsilon} > 0 \) is the weight for this group. \( G \) is the number of groups, \( 1 \leq G \leq N \); \( \Delta \sigma_{g_{\epsilon}} \cap \Delta \sigma_{g_{\tau}} = \emptyset \) if \( \epsilon \neq \tau \), and \( \bigcup_{\epsilon=1}^{G} \Delta \sigma_{g_{\epsilon}} = \Delta \sigma \). \( \tau \), \( \zeta \) and \( \epsilon \) are group indicators. In general, the groups can overlap, which is depicted by the conditions: \( \Delta \sigma_{g_{\zeta}} \cap \Delta \sigma_{g_{\tau}} \neq \emptyset \) if \( \zeta \neq \tau \) or \( \Delta \sigma_{g_{\zeta}} \cap \Delta \sigma_{g_{\tau}} = \emptyset \) if \( \zeta \neq \tau \), and \( \bigcup_{\epsilon=1}^{G} \Delta \sigma_{g_{\epsilon}} = \Delta \sigma \). Nevertheless, Yang et al. only investigated the non-overlapping group sparsity for EIT image reconstruction.

The aforementioned regularization strategies introduce regularization into EIT image reconstruction by employing a penalty term. Another approach to incorporate regularization is through multiplicative regularization (van den Berg, Abubakar, & Fokkema, 2003). Zhang et al. introduce this approach into EIT and the cost functional \( C_{MR}(\Delta \sigma) \) of the difference reconstruction problem at the \( t^{th} \) iteration is formulated as (K. Zhang, Li, Yang, Xu, & Abubakar, 2019):

$$
C_{MR}^{t}(\Delta \sigma) = \frac{\| \Delta V - J \Delta \sigma \|^2}{\| \Delta V \|^2} \times \Phi_{t}(\Delta \sigma),
$$

where \( \Phi_{t}(\Delta \sigma) \) denotes the multiplicative regularization functional at the \( t^{th} \) iteration. Starting from an initial point of zero and iterating only once, the solution can be formulated as:

$$
\Delta \sigma^{*} = \left( \frac{2J^{T}J}{\| \Delta V \|^2} + L_{0} \right)^{-1} \frac{2J^{T}\Delta V}{\| \Delta V \|^2},
$$

where \( L_{0} \) is the discrete Laplace operator scaled by the number of tetrahedral elements in the adopted mesh. This scaling operation originates from the definition and discretization of the multiplicative regularization functional (K. Zhang et al., 2019). The results demonstrate such a parameter-free algorithm has a good reconstruction accuracy and anti-noise performance.

With the development of deep learning (DL), a new type of regularization strategy named Untrained Neural Network Priors (UNNPs) is proposed for the inverse problem. Unlike the traditional manually designed priors, this method uses a neural network as the regularizer to the inverse problem. The initial UNNP-based work was described in (Ulyanov, Vedaldi, & Lempitsky, 2018), which established a new connection between the inverse problem and DL. Subsequent research has proposed various UNNP-based approaches (Gandelsman, Shocher, & Irani, 2019; Heckel & Hand, 2018; Qayyum, Sultani, Shamshad, Tufail, & Qadir, 2022). In the context of EIT, Liu et al. introduced the UNNP-based method for 2D reconstruction (D. Liu et al., 2023). In their algorithm, the EIT nonlinear forward model (2.7) is adopted.
and the EIT inverse problem is formulated as:

\[
\hat{\theta} = \arg \min_{\theta} \| F(P(\theta(Z))) - V \|^2, \quad \hat{\sigma} = P(f_{\hat{\theta}}(Z)),
\] (2.20)

where \( \hat{\sigma} \) is the estimated discrete conductivity distribution. \( f_{\theta}(Z) \) denotes a deep convolutional neural network whose parameters are \( \theta \) and whose input is \( Z \). \( P \) is a mapping between the measurement domain and the image domain. Their results showed superior shape preservation ability compared to conventional hand-crafted regularization-based algorithms.

**Learning-based Algorithms**

Recently, deep learning (DL) has revolutionized research into inverse problems. DL-based methods offer significantly improved image quality and rapid inference times, and they have demonstrated remarkable effectiveness and efficiency in automatically extracting the inverse operator from extensive datasets (G. Wang, Ye, & De Man, 2020). Drawing inspiration from the unprecedented success of deep learning in the domain of CT/PET/MRI image reconstruction, the utilization of deep learning in EIT image reconstruction signifies an emerging frontier (T. Zhang et al., 2022). The majority of learning-based image reconstruction approaches can be classified into three primary groups.

**Pure Learning:** These methods, propelled by extensive datasets, directly learn the inverse mapping from measured EIT data to conductivity images through a neural network. These networks typically adopt the feed-forward architecture, which consists of convolutional layers, fully connected layers, and activation functions (Chen et al., 2020; F. Li et al., 2020; Tan et al., 2018). To deal with time-serials EIT measurements, Recurrent Neural Network (RNN) architecture was also investigated (Ren, Guan, Liang, & Dong, 2021). Unlike the reliance on mathematical and physical models, this approach is entirely data-driven. The neural network is often perceived as a black box, with its performance heavily contingent on the quality, quantity, and diversity of the training data. Nevertheless, this dependence on training data can somewhat restrict its ability to generalize.

**Post-processing:** Rather than entirely disregarding physical insights, this approach starts with the initial conductivity images or certain intermediate quantities generated by the aforementioned model-based algorithms. For example, Hamilton et al. proposed to use U-Net as a post-processing method for deconvolving the convolved direct reconstructions of the D-bar method and demonstrated structure-enhanced EIT images (Hamilton et al., 2018). Wei et al. also adopted the U-Net architecture to process the neural network’s multichannel inputs originating from the dominant parts of the Induced Contrast Current (ICC) and produced quality-improved EIT images (Wei & Chen, 2019). In addition, a V-shaped dense denoising convolutional neural network was proposed to enhance the EIT images reconstructed using the model-based algorithm (X. Zhang et al., 2022). And Wang et al. designed a Convolutional
2.4. EIT Image Reconstruction Algorithms

Neural Network (CNN) to post-process the results of the model-based algorithm (Q. Wang, Zhang, et al., 2021). Learning-based post-processing still encounters similar challenges to fully learning-based algorithms; specifically, its performance is constrained by the quality, quantity, and diversity of the training data.

**Model-based Learning:** To bestow interpretability on DL-based algorithms, the concept of model-based learning is being explored. Instead of exclusively relying on either extensive datasets or pure physics, this emerging branch of learning-based unrolling approaches integrates deep neural networks with conventional iterative reconstruction algorithms. More precisely, it unravels the iterative steps of traditional algorithms into a sequential of blocks containing a deep network architecture, as demonstrated in paradigmatic methods such as MoDL (Aggarwal, Mani, & Jacob, 2018), ADMM-CSNet (Y. Yang, Sun, Li, & Xu, 2018), and FISTA-Net (Xiang, Dong, & Yang, 2021). In EIT, for instance, a Graph Convolutional Newton-type Method (GCNM) was proposed for solving EIT image reconstruction and the results illustrated a good generalization ability on distinct domain shapes and meshes (Herzberg, Rowe, Hauptmann, & Hamilton, 2021). An unrolled Gauss-Newton network was devised for EIT inversion, and the outcomes exhibited a notably enhanced reconstruction performance (Colibazzi, Lazzaro, Morigi, & Samoré, 2022).

### 2.4.2 Multi-Modal Algorithms

**Model-based Algorithms**

For the multi-modal system combining EIT, MIT, and ICEIT (Gursoy et al., 2011), the authors adopt the linearized forward model, i.e. \( \Delta V = J \Delta \sigma \). This equation is solved with the SVD-based reconstruction algorithm and the solution is expressed by \( \Delta \sigma = Y \Sigma_{q}^{\dagger} D^{T} \Delta V \), where the \( Y \) and \( D \) are singular vectors and \( \Sigma_{q}^{\dagger} \) represents the pseudoinverse of \( J \) with every nonzero entry replaced by its reciprocal. \( q \) denotes the truncation index.

With regard to the EIT-OPT joint reconstruction (Lehti-Polojärvi et al., 2021), the authors first segment the OPT image. They then incorporate the prior information into the EIT inversion by assuming the conductivity inside each segment is homogeneous. In their Bayesian-based work, the estimated conductivity at the frequency \( f \) is:

\[
\hat{\sigma}^f = \arg \min_{\sigma} \left\| L^f \left( V^f - F^f(\sigma, z) \right) + \mu^f \right\|^2,
\]

where \( F^f \) is the nonlinear forward model at the frequency \( f \). \( L^f \) is the Cholesky factor of the noise precision matrix. The detailed definition of the \( L^f \) can refer to (Lehti-Polojärvi et al., 2021). \( z \) denotes the contact impedance vector. \( \mu^f = F^f(\sigma_{ref}, z) - V_{ref}^f \), where \( \sigma_{ref} \) is the known homogeneous conductivity distribution and \( V_{ref}^f \) is the corresponding measurements.
2.4. EIT Image Reconstruction Algorithms

Both Gong et al. (Gong, Schulicke, Krueger-Ziolk, Mueller-Lisse, & Moeller, 2016) and Liu et al. (Z. Liu & Yang, 2021a) proposed to incorporate the prior information of the auxiliary image into EIT inversion through a non-overlapping group lasso. Specifically, the grouping rule for the $\Delta \sigma$ is designed based on the information provided by the auxiliary image. In this scenario, the group lasso term in (2.17) serves as the means of introducing the prior information. The distinction lies in Gong et al. using K-Means clustering over auxiliary image pixels to formulate the grouping rules, while Liu et al. create grouping rules based on semantic segmentation results of the auxiliary image.

Another approach proposed by Li et al. involved encoding structural information from the CT image using Cross-Gradient regularization (Z. Li et al., 2019). The Cross-Gradient regularization is designed for geophysical imaging. It aids in preserving similarity among distinct physical properties while permitting varying magnitudes for each property value within the shared imaging area (Gallardo & Meju, 2003). Li et al. utilized the resultant regularization term to constrain the EIT inversion process. Their EIT image reconstruction is formulated as:

$$\min_{\Delta \sigma} \| J \Delta \sigma - \Delta V \|^2 + \| \alpha T \Delta \sigma \|^2 + \| \beta \mathcal{C}(\Delta \sigma, m) \|^2,$$

where $\alpha$ and $\beta$ represent the parameters for Tikhonov regularization and Cross-Gradient regularization, respectively. $T$ is the Tikhonov regularization matrix and $\mathcal{C}(\Delta \sigma, m)$ stands for the Cross-Gradient vector between the conductivity distribution $\Delta \sigma$ and the CT image $m$. Their results demonstrate structure-enhanced EIT images. Although several multi-modal algorithms are reviewed, it should be noted that the number of multi-modal algorithms is much fewer than that of single-modal algorithms.

Learning-based Algorithms

Currently, limited literature exists on learning-based multi-modal EIT image reconstruction. Liu et al. (Z. Liu, Bagnaninchi, & Yang, 2021) introduced a pioneering study on dual-modal EIT imaging for 3D cell culture. This approach employs an impedance-optical sensor, a guidance image processing algorithm set, and a deep learning model called Multi-Scale Feature Cross Fusion Network (MSFCF-Net). The impedance-optical sensor provides voltage measurements and a high-resolution guidance image containing structural details. The guidance image processing algorithm generates a low-resolution binary mask image from the guidance image. The trained MSFCF-Net then reconstructs EIT images using the mask image and voltage measurements. Extensive simulations demonstrate the superiority of this dual-modal approach over single-modal model-based and learning-based methods. The proposed framework excels in preserving structure and predicting conductivity due to the inclusion of structural information. The method’s effectiveness is validated through imaging MCF-7 cell aggregates in real scenarios.
2.4. EIT Image Reconstruction Algorithms

The reconstructed EIT image quality from (Z. Liu et al., 2021) depends on the accuracy of the segmented mask image. Factors affecting mask image quality include measurement errors, imaging conditions, and guidance image processing. These factors are imperfect in real applications, leading to unavoidable mask image inaccuracies. To address this, Liu et al. introduced a two-stage neural network, the Enhanced Multi-Scale Feature Cross-Fusion Network (En-MSFCF-Net), in (Z. Liu, Zhao, Anderson, Bagnaninchi, & Yang, 2022). This network integrates inaccurate mask image correction and EIT image reconstruction sequentially, enhancing interpretability. En-MSFCF-Net's performance is assessed both qualitatively and quantitatively in simulations, demonstrating effective boundary preservation and internal conductivity homogeneity for inclusions. Experimental studies involving black resin, mango, and hydrogel imaging further validate En-MSFCF-Net's effectiveness.

2.5 EIT Applications in Tissue Engineering

Due to its non-invasive, non-radiative properties, and high temporal resolution, EIT offers unique advantages in biomedical engineering. For example, EIT has been found applications in breast cancer screening (Choi, Kao, Isaacson, Saulnier, & Newell, 2007; Sadleir, Sajib, Kim, Kwon, & Woo, 2013), nerve imaging (Aristovich et al., 2018; Ravagli et al., 2020), stroke detection (Goren et al., 2018; McDermott et al., 2020; L. Yang et al., 2017), brain tumor diagnosis (Romsauerova et al., 2006) and so forth. This thesis primarily focuses on EIT for tissue engineering, specifically 3D cell culture imaging.

The feasibility of EIT for tissue imaging relies on the frequency-dependent conductivity of the tissues. It is widely reported that frequency-dependent electrical properties of biological cells and tissues depend on the morphological, pathological, and physiological status of cells and tissues (Miklavčič et al., 2006; R. Pethig & Kell, 1987; Schwan, 1994). A simple model only considers the interfacial polarization, and the electrical properties of tissues depend on stimulation frequencies, cells, and extracellular matrices (Hanai, 1960; Heileman, Daoud, & Tabrizian, 2013; Schwan, 1994). The current cannot flow through the cell membranes at low frequencies as the cell membranes demonstrate high resistance, while the current is able to pass through the cells because of the high capacitance of the cell membranes at high frequencies (Markx, 2008). At extremely high frequencies, the current has no time to flow and only bounces back and forth between the internal and external surfaces of the cellular membranes (Dean, Ramanathan, Machado, & Sundararajan, 2008; Pliquett & Prausnitz, 2000).

Considering a more general case and sweeping frequencies from 1 Hz to 10 GHz, the dielectric properties of tissues are mainly characterized by three dispersions: α-dispersion, β-dispersion, and γ-dispersion (see Fig. 2.4). The α-dispersion is mainly associated with ionic species diffusion, which is correlated with the cellular membrane potential Prodan, Mayo, Claycomb, Miller Jr, and Benedik (2004), gap junctions (Stoy, Foster, & Schwan, 1982) and
The β-dispersion is mainly related to the interfacial polarization of the membranes (Z. Jiang et al., 2019; Y. Xu et al., 2016). The γ-dispersion is caused by the presence of water contents (Foster & Schwan, 2019; Stoy et al., 1982). In addition, there is another minor dispersion called δ-dispersion, which is correlated with the dipolar moments of proteins and other large molecules and protein-bound water (Asami, 2002; Gotz, Karsch, & Pawelke, 2017; R. R. Pethig, 2017). There are many models demonstrating the mathematical relationship between the electrical properties of tissues and the frequencies, such as the Debye equation (Debye, 1929) and a more general Cole–Cole equation (Cole & Cole, 1941). Research on determining the parameters of these equations has also been studied (Gabriel, Lau, & Gabriel, 1996; Hill, 1969).

Nevertheless, the aforementioned evidence motivates that the imaging parameters of EIT can be modeled by a complex conductivity $\sigma_\omega^e(p) = \sigma_\omega(p) + j\omega\varepsilon_\omega(p)$, where $\sigma_\omega(p)$ is the ohmic conductivity, $\varepsilon_\omega(p)$ is the permittivity, $p$ is the position vector and $\omega = 2\pi f$ is the angular frequency (Jun et al., 2009; Seo, Lee, Kim, Zribi, & Woo, 2008). In the context of EIT imaging, physiological or pathological variations of tissues can change their complex conductivity $\sigma_\omega^e(p)$. For example, in lung imaging, constitutive model and experiments demonstrate the linear relationship between the alveolar air content and the resistivity (Roth et al., 2015). Muscular fatigue and ischemia can change the chemical and pH of tissues, leading to the change of $\sigma_\omega^e(p)$ Packham et al. (2012). These observations inspire the broad applications of EIT.
2.5. EIT Applications in Tissue Engineering

Based on the aforementioned evidence, applications of EIT in 3D cell culture have been widely reported. For instance, Wu et al. proposed the use of EIT for the quantitative assay of cell spheroids. They verified the effectiveness of EIT in cell monitoring through single-shell cell model simulations and real experiments. In these real experiments, the authors exposed the cells to Triton X-100 to monitor their viability (Wu, Yang, et al., 2018). The results demonstrated high consistency with the conventional cellular metabolic viability assays. Furthermore, Wu et al. applied both time-difference EIT and frequency-difference EIT to image cells that are cultivated in hydrogel and microporous scaffolds (Wu, Zhou, Yang, Jia, & Bagnaninchi, 2018). Their results proved the effectiveness of EIT in monitoring cells in hydrogel and microporous scaffolds. The same authors then proposed a method named calibrated frequency-difference EIT (CFDEIT) for 3D tissue culture imaging (Wu, Yang, Bagnaninchi, & Jia, 2019). Their results demonstrated that CFDEIT is more suitable for 3D tissue culture compared with conventional frequency-difference EIT. In addition, a 16-electrode EIT sensor was designed for 3D cell aggregates (Yin et al., 2018), and a miniature EIT sensor was proposed for scaffold-based 3D cell culture (Y. Yang et al., 2019). These results further demonstrate the potential of EIT for label-free, non-destructive, real-time monitoring of 3D cells.

These studies have provided compelling evidence supporting the prospective use of EIT in the realm of 3D cell culture monitoring. This innovative technique has opened new avenues for observing cellular behaviors and interactions within three-dimensional cultures, offering invaluable insights into the dynamic processes of these complex systems. It is worth mentioning that various tissues and 3D cells can be selected as study subjects. However, two main challenges exist. The first challenge is sensor micro-miniaturization, which has resulted in significantly weaker measurement signals and increased sensitivity to sensor imperfections. Addressing this challenge necessitates sensor optimization to obtain robust, high-quality image reconstruction. The second challenge lies in the intrinsic limitation of EIT’s spatial resolution, which hampers the quantitative analysis of tissue status. Consequently, adopting a multi-modal imaging approach holds significant promise for advancing tissue engineering.

2.6 Summary

This chapter provides a concise introduction to the principle of EIT, diverse EIT-incorporated multi-modal systems, single-modal and multi-modal EIT image reconstruction algorithms, and the application of EIT in tissue engineering. The Chapter’s objective is to underscore the potential of EIT within tissue engineering and to address the primary challenge that EIT faces in this context: its limited spatial resolution. Consequently, these discussions prompt an exploration of multi-modal methodologies in the realm of tissue engineering. As a result, the innovative contribution of this thesis becomes apparent in the development of a multi-modal imaging pipeline that encompasses a range of multi-modal algorithms. Subsequent chapters will present this pipeline and algorithms in detail.
3.1 Introduction

The low spatial resolution of Electrical Impedance Tomography (EIT) makes it challenging to conduct quantitative analysis of the electrical properties of imaging targets in biomedical applications. From the viewpoint of the images, the accurate recovery of conductivity levels and shapes remains a significant challenge for EIT.

This chapter proposes an EIT-optical dual-modal imaging approach to address the aforementioned challenges. We introduce Image-Guided Group Sparsity (IGGS) for information fusion and high-quality conductivity reconstruction by leveraging the EIT measurements and microscopic images from a miniature impedance-optical dual-modal sensor as input. IGGS provides a new way to incorporate the structural information contained in the microscopic image into EIT image reconstruction by using the group sparsity regularization, which has been comprehensively investigated in single-modal EIT image reconstruction (Y. Yang & Jia, 2017a; Y. Yang et al., 2017). IGGS adopts pixel grouping to link group sparsity with the structural information extracted from microscopic image segmentation. The finally established optimization problem is solved by the Accelerated Alternating Direction Method of Multipliers (A-ADMM) (Goldstein, O’Donoghue, Setzer, & Baraniuk, 2014). The results of the proposed method and the given single-modal based algorithms, i.e. Tikhonov regularization (TReg) (Vauhkonen et al., 1998), Structure-Aware Sparse Bayesian Learning (SA-SBL) (S. Liu, Jia, Zhang, & Yang, 2018) and Enhanced Adaptive Group Sparsity with Total Variation (EAGS-TV) (Y. Yang et al., 2017), are thoroughly compared by simulation and real-world experiments.
3.2 EIT-optical Dual-modal Sensor

The manufactured dual-modal sensor is shown in Fig. 3.1. It comprises a miniature 16-electrode EIT sensor and a digital microscope (Digital USB Microscope 1.3M, RS Components Ltd). The EIT sensor is placed under the microscope and the two sensors share the same sensing region. We select two different EIT sensors to investigate our method. They are labeled as EIT sensor A (see Fig. 3.2 (a)) and EIT sensor B (see Fig. 3.2 (b)). The two EIT sensors are both manufactured on the Printed Circuit Board (PCB).

The sensing area of EIT sensor A is bounded by the PCB board (bottom of the sensing area) and a transparent glass tube (see Fig. 3.2 (a)). The height and the inner diameter of the glass tube are 6 mm and 15 mm, respectively. Sixteen gilded square microelectrodes are manufactured on the surface of the PCB and uniformly distributed at the bottom of the sensing area.

The imaging targets in EIT sensor B are placed on the transparent glass substrate at the bottom of the sensing domain (see Fig. 3.2 (b)). The sidewall of the sensing region is surrounded by the PCB and microelectrodes. The height of microelectrodes is the same as the thickness of the PCB, i.e. 1.6 mm. The diameter of the sensing area is 15 mm. Sixteen gilded microelectrodes are manufactured using the half-hole process and uniformly distributed at the periphery of the sensing area.

3.3 Image-Guided Group Sparsity (IGGS)

IGGS consists of three steps (see Fig. 3.1). In the first step (semantic segmentation), the input RGB microscopic image is converted into its binary version. The height and width of the converted binary image (named mask image) is the same as those of the EIT image. In the second step (pixel grouping), the pixels of the EIT image are partitioned into different groups based on the mask image. In the last step (optimization solving), the grouping result first navigates the construction of the group sparsity regularization term. Afterwards, the final optimization problem will be established and solved by the Accelerated Alternating Direction Method of Multipliers (A-ADMM) (Goldstein et al., 2014). Each step of IGGS is described as follows.
3.3. Semantic Segmentation

The purpose of semantic segmentation is to generate the mask image of the input microscopic image. The algorithm in this step is replaceable because it highly depends on the configuration of the dual-modal sensor and the application of the imaging system. As stated in Section 3.2, there are two EIT sensors to conduct experiments in this work and they possess disparate structures, which leads to distinct types of microscopic images. For example, electrodes usually appear in the microscopic image generated by EIT sensor A-based dual-modal sensor, while this situation does not happen in the microscopic image generated by EIT sensor B-based dual-modal sensor. Thus, the electrodes should be eliminated in the semantic segmentation for images based on EIT sensor A-based dual-modal sensor. Therefore, different sets of semantic segmentation algorithms should be applied to these sensors, and each set of algorithms includes multiple image operations.

The first set of segmentation algorithms is developed for the EIT sensor A-based dual-modal sensor. In operation 1 (OPA1), an RGB difference image is generated by subtracting the calibration image from the carrot image. The calibration image can be collected before real-time imaging and there are no imaging targets in the calibration image. In operation 2 (OPA2), the RGB difference image is first converted into its grayscale version. Then, Otsu’s method-based segmentation algorithm is applied to this grayscale image to transform it into a binary image. Otsu’s method, as a histogram-based technique, separates an image into two classes, i.e. foreground and background, by finding the global grayscale value threshold that maximizes the variance between these classes (Otsu, 1979). According to the calculated grayscale value threshold, pixels with the value above the threshold will be transformed to white (digit 1) and
3.3. Image-Guided Group Sparsity (IGGS)

Figure 3.2: Structure of (a) EIT sensor A and (b) EIT sensor B.

Other pixels will be transformed to black (digit 0). The formula of Otsu’s method for threshold searching is expressed as:

\[ t^* = \arg \min_{1 \leq t \leq L} \frac{\left( \sum_{l=1}^{t} p_l \right) \left( \sum_{l=1}^{t} p_l \right) - \left( \sum_{l=1}^{L} p_l \right)^2}{\left( \sum_{l=1}^{t} p_l \right) \left( 1 - \sum_{l=1}^{L} p_l \right)}, \tag{3.1} \]

where \( t^* \) is the optimal threshold of a grayscale image. \( L \) is the total gray levels of this image and \( p_l = \frac{q_l}{n} \); \( q_l \) is the number of pixels at \( l^{th} \) gray level and \( n \) is the total number of pixels of the image.

In operation 3 (OPA3), open operation and dilation operation are applied successively to the binary image generated by OPA2 to refine the object’s boundary. Then, the result is downsampled to the EIT image size. Operation 4 (OPA4) is to eliminate small connected white regions to acquire the ultimate mask image. The threshold pixel number for the small connected white region is based on specific applications. This parameter is set as 50 throughout the paper. The two morphological operations in OPA3 are defined as (Gonzales & Wintz, 1987):

\[ I \circ S = \bigcup \{ (S)_z \mid (S) \subseteq I \} \tag{3.2} \]
\[ I \oplus S = \bigcup \{ z \mid (\hat{S}) \cap I \neq \phi \}, \tag{3.3} \]

where, \( I \circ S \) means image \( I \) is opened by the structuring element \( S \) and \( I \oplus S \) means \( I \) is dilated by \( S \). \( (S)_z \) and \( (\hat{S})_z \) are defined as:

\[ (S)_z = \{ k \mid k = \psi + z, \ \psi \in S \} \tag{3.4} \]
\[ \hat{S} = \{ \theta \mid \theta = -\psi, \ \psi \in S \}, \tag{3.5} \]

where \( z = (z_1, z_2) \) is a fixed point in the image. Fig. 3.3 provides an example of the first semantic segmentation procedure.
3.3. Image-Guided Group Sparsity (IGGS)

Figure 3.3: An example of semantic segmentation for EIT sensor A-based dual-modal sensor. The leftmost images are carrot image (bottom) and calibration image (top), and the rightmost image is the mask image. Numbers mean the pixel numbers of the side of the circumscribed square region.

Figure 3.4: An example of semantic segmentation for EIT sensor B-based dual-modal sensor. The leftmost image is the cell spheroid image and the rightmost image is the mask image. Numbers mean the pixel numbers of the side of the circumscribed square region.

The second set of segmentation algorithms is applied to EIT sensor B-based dual-modal sensor and it also includes four operations. Operation 1 (OPB1) is to obtain the one-dimensional illuminant invariant image of the microscopic image by using the method of Finlayson et al. (Finlayson, Drew, & Lu, 2009). This operation will convert the original RGB image into a grayscale version meanwhile removing the influence of illumination. The equation is defined as:

\[ I^{inv}(r, c) = \exp(\Gamma_1(r, c)\cos(\theta) + \Gamma_2(r, c)\sin(\theta)), \]  

where \( r \) and \( c \) are pixel position indexes of an image. \( \theta \) is the projection direction in the two-dimensional log-chromaticity space of the microscopic image and it is a constant for a specific camera. This direction can be estimated by traversing every integer angle from \( 1^\circ \) to \( 180^\circ \) and it makes \( I^{inv} \) having the minimum Shannon’s entropy (Finlayson et al., 2009). \( \Gamma_1(r, c) \) and \( \Gamma_2(r, c) \) is calculated by:

\[
[\Gamma_1(r, c), \Gamma_2(r, c)]^T = [v_1, v_2]^T \kappa(r, c),
\]

where \( v_1 = [\frac{1}{\sqrt{2}}, -\frac{1}{\sqrt{2}}, 0]^T, v_2 = [\frac{1}{\sqrt{6}}, \frac{1}{\sqrt{6}}, -\frac{2}{\sqrt{6}}]^T, \kappa(r, c) \) is defined by:

\[
\kappa(r, c) = \left[ \ln\left( \frac{R(r, c)}{A(r, c)} \right), \ln\left( \frac{G(r, c)}{A(r, c)} \right), \ln\left( \frac{B(r, c)}{A(r, c)} \right) \right]^T
\]
3.3. Image-Guided Group Sparsity (IGGS)

where \( \Lambda(r, c) = \sqrt{R(r, c)G(r, c)B(r, c)} \), \( R(r, c) \), \( G(r, c) \), and \( B(r, c) \) are the three components of a color image.

In operation 2 (OPB2), the binary version of \( I^{inv} \) can be generated by using the following simple thresholding segmentation method:

\[
I^{bw}(r, c) = \begin{cases} 
0, & \text{if } I^{inv}(r, c) < \tau \\
1, & \text{if } I^{inv}(r, c) \geq \tau,
\end{cases}
\] (3.9)

where \( I^{bw} \) denotes the binary image after thresholding and \( \tau \) is selected based on empirical trials. Operation 3 (OPB3) uses the same two successive morphological operations as in OPA3 for the same purpose of refining object boundaries. Finally, in operation 4 (OPB4), the mask image is gained by down-sampling the result of OPB3 into the EIT image size. An example of the second segmentation algorithm is illustrated in Fig. 3.4.

3.3.2 Pixel Grouping

Based on the mask image, EIT image pixels in the same connected white region of the mask image will be considered to have a similar structure and are labelled as the same large group. The other individual pixels will be labelled as small groups. Examples of grouping results can be found in Table III. It should be noted that each large group contains more than one pixel, and each small group only contains one pixel. Suppose the pixels of the EIT image can be classified into \( N \) groups, the underlying conductivity change can be expressed as:

\[
\Delta \sigma = \{ \Delta \sigma_{g1}, \Delta \sigma_{g2}, \ldots, \Delta \sigma_{gN} \} 
\] (3.10)

where \( g_i, i = 1, 2, \ldots, N \), represents group index of the \( i^{th} \) group. This expression should satisfy the properties of \( \Delta \sigma = \bigcup_{i=1}^{N} \Delta \sigma_{g_i} \) and \( \Delta \sigma_{g_i} \cap \Delta \sigma_{g_j} = \emptyset \) for any \( i \neq j \).

3.3.3 Optimization Solving

The key idea of IGGS is to incorporate structural information from the optical image by using group sparsity regularisation. Group sparsity groups pixels with structural similarities and apply sparsity constraint on the formed pixel groups. Therefore, the grouping result from the second step of IGGS will guide the formulation of the group-level regularisation term. The vanilla form of group sparsity can be expressed by the following \( l_{2,1} \) norm (Huang & Zhang, 2010):

\[
||\Delta \sigma||_{2,1} = \sum_{i=1}^{N} ||\Delta \sigma_{g_i}||_2.
\] (3.11)
In this work, we adopt weighted group sparsity, and the ultimate optimization problem for IGGS based on weighted group-level constraint and Total Variation (TV) constraint can be formulated by the below equations:

\[
\begin{aligned}
    \min_{\Delta \sigma} & \quad \sum_{i=1}^{N} \omega_i ||\Delta \sigma_{g_i}||_2 + ||\Delta \sigma||_{TV} \\
    \text{s.t.} & \quad J \Delta \sigma = \Delta V,
\end{aligned}
\]  

(3.12)

where \(J\) denotes the sensitivity matrix. \(\sum_{i=1}^{N} \omega_i ||\Delta \sigma_{g_i}||_2\) is the weighted \(l_{2,1}\) norm and \(\omega_i\) is the weight for \(i^{th}\) group. \(||\Delta \sigma||_{TV}\) is the isotropic TV norm, which can help smooth the estimated EIT image and is defined as (Chambolle, 2004):

\[
||\Delta \sigma||_{TV} = \sum_{r,c} \sqrt{(D_{hr}(\Delta \sigma))^2 + (D_{vr}(\Delta \sigma))^2}
\]  

(3.13)

where \(D_{hr}(\Delta \sigma)\) and \(D_{vr}(\Delta \sigma)\) are the first order finite difference operators in the horizontal direction and vertical direction, respectively. And these two operators are defined by (3.14) and (3.15), respectively:

\[
D_{hr}(\Delta \sigma) = \begin{cases}
\Delta \sigma_{r,c} - \Delta \sigma_{r,c+1}, & 1 \leq c < h_n \\
0, & c = h_n
\end{cases}
\]

(3.14)

\[
D_{vr}(\Delta \sigma) = \begin{cases}
\Delta \sigma_{r,c} - \Delta \sigma_{r+1,c}, & 1 \leq r < v_n \\
0, & r = v_n
\end{cases}
\]

(3.15)

where \(h_n\) denotes the pixel number along the horizontal direction and \(v_n\) denotes the pixel number along the vertical direction. To solve (3.12), the accelerated ADMM (A-ADMM) is used, which exhibits faster convergence than the conventional ADMM by including an over-relaxation step (Goldstein et al., 2014). By introducing an auxiliary vector, \(a\), (3.12) can be equivalently rewritten as:

\[
\begin{aligned}
    \min_{\Delta \sigma} & \quad \sum_{i=1}^{N} \omega_i ||a_{g_i}||_2 + ||\Delta \sigma||_{TV} \\
    \text{s.t.} & \quad a = \Delta \sigma, \ I \Delta \sigma = \Delta V,
\end{aligned}
\]  

(3.16)
3.3. Image-Guided Group Sparsity (IGGS)

Equation (3.16) can be solved by the augmented Lagrangian scheme and its equivalent augmented Lagrangian problem is formulated as:

$$\min_{\Delta \sigma, a} \sum_{i=1}^{N} \omega_i \|a_{gi}\|_2 + \|\Delta \sigma\|_{TV} - \lambda_1^T (a - \Delta \sigma) + \frac{\eta_1}{2} \|a - \Delta \sigma\|_2^2 - \lambda_2^T (J \Delta \sigma - \Delta V) + \frac{\eta_2}{2} \|J \Delta \sigma - \Delta V\|_2^2$$

(3.17)

where $\lambda_1$ and $\lambda_2$ represents multipliers; $\eta_1$ and $\eta_2$ are penalty parameters. In the A-ADMM framework, (3.17) is decomposed into the following $\Delta \sigma$-subproblem (3.18) and $a$-subproblem (3.19), and these two subproblems can be solved separately.

$$\Delta \sigma^{k+1} = \arg \min_{\Delta \sigma} \left\{ \|\Delta \sigma\|_{TV} + (\lambda_1^k)^T \Delta \sigma + \frac{\eta_1}{2} \|a^k - \Delta \sigma\|_2^2 - (\lambda_2^k)^T J \Delta \sigma + \frac{\eta_2}{2} \|J \Delta \sigma - \Delta V\|_2^2 \right\}$$

(3.18)

$$a^{k+1} = \arg \min_{a} \left\{ \sum_{i=1}^{N} \omega_i \|a_{gi}\|_2 - (\lambda_1^k)^T a + \frac{\eta_1}{2} \|a - \Delta \sigma^k\|_2^2 \right\}$$

(3.19)

The $\Delta \sigma$-subproblem (3.18) is solved by a gradient-based recovery algorithm, and each iteration equation is expressed as:

$$\Delta \sigma^{k+1} = \Delta \sigma^k - \mu \left\{ J^T \left( \eta_2 J \Delta \sigma^k - \eta_2 \Delta V - \lambda_2 \right) + \lambda_1 + \eta_1 \left( \Delta \sigma^k - a \right) + \nabla \|\Delta \sigma^k\|_{TV} \right\}$$

(3.20)

where $\mu$ is the iteration step length, and the gradient of TV norm based on a smooth approximation strategy is calculated by:

$$\nabla_{r,c} \|\Delta \sigma\|_{TV} = \frac{D_{r,c}^b (\Delta \sigma) + D_{r,c}^c (\Delta \sigma)}{\sqrt{(D_{r,c}^b (\Delta \sigma))^2 + (D_{r,c}^c (\Delta \sigma))^2 + \varphi}}$$

$$- \frac{D_{r,c-1}^b (\Delta \sigma)}{\sqrt{(D_{r,c-1}^b (\Delta \sigma))^2 + (D_{r,c-1}^c (\Delta \sigma))^2 + \varphi}}$$

$$- \frac{D_{r-1,c}^c (\Delta \sigma)}{\sqrt{(D_{r-1,c}^b (\Delta \sigma))^2 + (D_{r-1,c}^c (\Delta \sigma))^2 + \varphi}}$$

(3.21)

where $\varphi$ is the relaxation factor, which can avoid the occurrence of zero denominator in the gradient of TV norm and should not be too large. $\varphi$ is set as $1 \times 10^{-7}$ throughout this paper based on a series of trials.
3.3. Image-Guided Group Sparsity (IGGS)

The \(a\)-subproblem ((3.19)) is solved by the below group-wise soft thresholding (Deng, Yin, & Zhang, 2013):

\[
\mathbf{a}_{g_i} = \max \left\{ \left\| \Delta \mathbf{\sigma}_{g_i} + \frac{1}{\eta_1} (\lambda_1)_{g_i} \right\|_2 \right. - \frac{\omega_i}{\eta_1}, 0 \} \frac{\Delta \mathbf{\sigma}_{g_i} + \frac{1}{\eta_1} (\lambda_1)_{g_i}}{\left\| \Delta \mathbf{\sigma}_{g_i} + \frac{1}{\eta_1} (\lambda_1)_{g_i} \right\|_2}.
\]  

(3.22)

After solving the \(\Delta \mathbf{\sigma}\)-subproblem and \(a\)-subproblem successively, an additional constraint is posed on the solution of the \(a\)-subproblem followed by the updates of multipliers based on the accelerated method. The additional constraint can improve the algorithm’s ability of voltage noise resistance and is defined as:

\[
\text{AP}_{i=1}^{N_i} \left( \text{sign}_{g_i} (\text{sum}_{g_i} (a)) \right) \cdot a \geq 0,
\]  

(3.23)

where \(\text{sum}_{g_i}()\) denotes the summation of all elements of \(a_{g_i}\). \(\text{sign}_{g_i}()\) means the operation of assigning the value of \(\text{sign}(\text{sum}_{g_i} (a))\) to each pixel of \(i^{th}\) group; here, \(\text{sign}()\) is the sign function. \(\text{AP}_{i=1}^{N_i}()\) means applying \(\text{sign}_{g_i} (\text{sum}_{g_i} (a))\) to all groups. This constraint imposes a non-negative constraint to the groups with the number one resulting from \(\text{sign}_{g_i} (\text{sum}_{g_i} (a))\) and imposes non-positive constraint to the groups with the number minus one resulting from the same equation. By this approach, it is expected that the artifact around the imaging targets can be effectively eliminated. Then, the update of multipliers based on the accelerated method is carried out according to the following equations:

\[
\begin{align*}
\lambda_1^{k+1} &= \lambda_1^k - \epsilon_1 \eta_1 (a^{k+1} - \Delta \mathbf{\sigma}^{k+1}) \\
\lambda_2^{k+1} &= \lambda_2^k - \epsilon_2 \eta_2 (\mathbf{1} \Delta \mathbf{\sigma}^{k+1} - \Delta V) \\
d_{k+1} &= 1 + \sqrt{1 + 4 (d^k)^2} \\
a^{k+1} &= a^{k+1} + \frac{2}{d_{k+1} - 1} (a^{k+1} - a^k) \\
\lambda_1^{k+1} &= \lambda_1^k + \frac{d_{k+1} - 1}{d_{k+1}^2} (\lambda_1^{k+1} - \lambda_1^k) \\
\lambda_2^{k+1} &= \lambda_2^k + \frac{d_{k+1} - 1}{d_{k+1}^2} (\lambda_2^{k+1} - \lambda_2^k)
\end{align*}
\]  

(3.24)

where, \(\epsilon_1\) and \(\epsilon_2\) are the iteration step lengths. \(d\) is an additional variable for the predictor-corrector–type acceleration process and its initial value is set as 1 throughout the paper.
3.3. Image-Guided Group Sparsity (IGGS)

**Algorithm 1:** Image-Guided Group Sparsity (IGGS)

**Input:** Sensitivity matrix $\mathbf{J}$, voltage change measurements $\Delta \mathbf{V}$, weight vector $\omega$, $\eta_1$, $\eta_2$, $\epsilon_1$, and $\epsilon_2$.

1. **Initialization:** $\Delta \sigma$ equals to the result of Tikhonov regularization. $a = \Delta \sigma$, $\lambda_1 = 0$, $\lambda_2 = 0$, $d = 1$.

2. **Step 1:** Semantic segmentation for guidance image by the application-specific algorithm.

3. **Step 2:** Pixel grouping according to the method depicted in section III-B-2).

4. **Step 3:** Iteration until satisfying stopping criteria, **Do**:
   1. Solve subproblem (3.18) by using (3.20).
   2. Solve subproblem (3.19) by using (3.22).
   3. Apply constraint (3.23) to the result of the step 2.
   4. Update multipliers by using (3.24).

**End Do.**

**Output:** The estimated conductivity change distribution.

IGGS adopts two stopping criteria in solving (3.12), i.e. the maximum iteration number and the below condition:

$$\|\Delta \sigma^{k+1} - \Delta \sigma^k\|_2 < \phi$$

where, $\phi$ is the tolerance. The IGGS will stop if either of the two criteria is satisfied. In addition, throughout the paper, weights selection is based on the following equation, which can promote the sparsity for large group conductivity estimation (Y. Yang & Jia, 2017a).

$$\omega_i = \begin{cases} 
\frac{1}{2N_s + N_l} & \text{if } \hat{i}^h \text{ group is large} \\
\frac{2}{2N_s + N_l} & \text{if } \hat{i}^b \text{ group is small}
\end{cases}$$

where $N_s$ and $N_l$ are the number of small groups and the number of large groups, respectively. They also satisfy $N_s + N_l = N$, $N$ is the number of total groups.

To sum up, the implementation of the whole IGGS algorithm is illustrated in **Algorithm 1**.
3.4 Results and Discussion

The proposed IGGS algorithm is evaluated by numerical simulation and real-world experiments. The performance of IGGS is compared with that of other widely used single-modal-based EIT image reconstruction algorithms, i.e. the classical Tikhonov regularization-based algorithm (TReg) (Vauhkonen et al., 1998) and the state-of-the-art Structure-Aware Sparse Bayesian Learning (SA-SBL) (S. Liu et al., 2018) and Enhanced Adaptive Group Sparsity with Total Variation (EAGS-TV) (Y. Yang et al., 2017) algorithms. The numerical simulation aims to quantitatively evaluate the performance of the algorithms and real-world experiments are to verify the practical feasibility.

3.4.1 Numerical Simulation

Modelling

A 16-electrode EIT sensor is modelled in COMSOL Multiphysics (see Fig. 3.5 (a)). The diameter of the sensor is 15 mm and the background medium is set as homogeneous saline with a conductivity value of 0.05 S/m−1. The material of electrodes is set as Titanium whose conductivity is $7.407 \times 10^5$ S/m−1. From Fig. 3.5 (b) to Fig. 3.5 (d), three types of conductivity distribution, i.e. phantom 1 to phantom 3, are modeled. The background material of all phantoms is saline with a conductivity value of 0.05 S/m−1. Phantom 1 simulates a large circle object with a conductivity value of 0.035 S/m−1. Phantom 2 simulates three dispersed small objects, i.e. two circles with conductivity values of 0.035 S/m−1 (upper left) and 0.015 S/m−1 (bottom left) respectively, and an ellipse object with conductivity value of 0.025 S/m−1. Phantom 3 simulates two square objects with conductivity values of 0.08 S/m−1 (upper right) and 0.035 S/m−1 (bottom) respectively. The adjacent sensing protocol is applied to obtain the boundary voltage data (Brown & Seagar, 1987).
3.4. Results and Discussion

Parameter Settings

The regularization factor of TReg is searched based on the L-curve method (Hansen & O’Leary, 1993). The calculated optimal regularization factors for phantom 1, phantom 2 and phantom 3 are $9.2140 \times 10^{-11}$, $2.5655 \times 10^{-6}$ and $1.1153 \times 10^{-6}$, respectively. Parameters of other algorithms are determined based on trial and error to ensure the best performance of the algorithms within a wide range of parameter sets. For all results based on SA-SBL, the maximum iteration number is set as 5 and the tolerance is selected as $1 \times 10^{-5}$; the pattern coupling factor and the cluster size are chosen as 0.3 and 4, respectively. For EAGS-TV and IGGS, the result of Treg with the regularization factor of 0.001 is selected as their starting point and the weight calculation is based on (3.26). The maximum iteration number of IGGS is set as 90 for phantom 1 and phantom 2 and set as 40 for phantom 3. The stopping tolerance of IGGS for all phantoms is set as $1 \times 10^{-7}$. The iteration number and stopping tolerance are set as 150 and $1 \times 10^{-7}$ for all cases based on EAGS-TV. For IGGS, the penalty parameters $\eta_1$ and $\eta_2$ are set as $0.0015/\text{mean}(\text{abs}(\Delta V))$ and $0.0005/\text{mean}(\text{abs}(\Delta V))$. $\text{abs}()$ converts each element of $\Delta V$ to its absolute value and the function of $\text{mean}()$ is to calculate the average value of the vector $\text{abs}(\Delta V)$. The multiplier update step lengths $\varepsilon_1$ and $\varepsilon_2$ are both selected as 0.4854. The two multiplier update step lengths for EAGS-TV are the same and are set as 0.9870. In EAGS-TV, the penalty parameter for the $l_2$ norm related to auxiliary variable is set as $1/\text{mean}(\text{abs}(\Delta V))$ and the penalty parameter for the $l_2$ norm related to EIT linearized model is set as $10/\text{mean}(\text{abs}(\Delta V))$. In addition, the maximum group diameter for EAGS-TV is set as 10 pixels, which is reasonable in this study. If not specified, algorithm parameter settings follow the above configuration in the following discussions.

Quantitative Metrics

In simulation, as the ground truth is known, the reconstructed image can be quantitatively evaluated by two metrics. The first one is the Relative Image Error (RIE), which aims to evaluate the accuracy of the predicted conductivity values and is defined as:

$$\text{RIE} = \frac{\|E - G\|_2}{\|G\|_2}. \quad (3.27)$$

The other metric is the Mean Structural Similarity Index (MSSIM) (Z. Wang, Bovik, Sheikh, & Simoncelli, 2004), which assesses the ability of the structure preservation. The expression of the MSSIM is:

$$\text{MSSIM} = \frac{1}{WH} \sum_{r} \sum_{c} \frac{(2\mu_E \mu_G + C_1)(2\delta_{EG} + C_2)}{(\mu_E^2 + \mu_G^2 + C_1)(\delta_E^2 + \delta_G^2 + C_2)}, \quad (3.28)$$
3.4. Results and Discussion

Figure 3.6: Comparison of different algorithms on different phantoms.

where $E$ and $G$ are the reconstructed image and the ground truth, respectively. $W$ and $H$ are the width and height of an image. $\mu_E = \mu_E(r, c)$, $\mu_G = \mu_G(r, c)$, $\delta_E = \delta_E(r, c)$, $\delta_G = \delta_G(r, c)$, and $\delta_E G = \delta_E G(r, c)$ are the local means, standard deviations and cross-covariance for $E$ and $G$. $C_1 = (K_1 L)^2$ and $C_2 = (K_2 L)^2$. $K_1$ and $K_2$ are constants with values of 0.01 and 0.03, respectively. As the absolute pixel values of the reconstructed EIT images in both simulation study and real-world experiments are normalized to [0, 1] in this work, $L$ is set as 1.

Result Comparison and Discussion

Fig. 3.6 displays the reconstructed EIT images, RIE and MSSIM based on IGGS, TReg, SA-SBL and EAGS-TV. In these results, the voltage data is noise-free and the mask image for IGGS is accurate and generated by assigning one to pixels where there are objects and assigning zero to the background pixels. The mask images and corresponding grouping results are shown in Fig. 3.7. In Fig. 3.7, LNG means the number of large groups and SNG means the number of small groups. When a mask image is given, the grouping results can be easily acquired by the method in Subsection 3.3.2. Thus, for later reconstructed images by IGGS, we only provide mask images. According to Table II, although TReg can predict
3.4. Results and Discussion

Figure 3.7: Mask images of phantoms and corresponding grouping results. The first row is mask images and the second row is the grouping results.

The position of objects correctly, the shape and conductivity contrasts are significantly wrong (see its images, RIE and MSSIM) and this algorithm suffers from severe background noise. SA-SBL and AGS-TV show considerable improvement in terms of the accuracy of the shape and conductivity contrasts. When the shape of the imaging objects are circle and ellipse, they can predict a relatively accurate shape. However, these two algorithms are powerless when encountering imaging objects with angles and straight lines like phantom 3 and the shape feature is lost. Differently, IGGS can generate the most accurate position, shape, and conductivity contrasts.

Fig. 3.8 selects phantom 2 to compare the noise resistance ability of algorithms with Signal-to-Noise Ratios (SNR) of 35 dB and 25 dB. Since the voltage data are changed, the regularization factors of TReg for phantom 2 should be re-calculated based on the L-curve method (Hansen & O’Leary, 1993). The searched regularization factors for voltage data with the SNR of 35 dB and 25 dB are $3.5384 \times 10^{-6}$ and $1.7933 \times 10^{-5}$, respectively. As shown in Fig. 3.6 and Fig. 3.8, EAGS-TV presents a good noise-resistance ability. The shape of objects in the reconstructed images of this algorithm does not change significantly and the RIE varies within 0.03. The performance of SA-SBL is worse than EAGS-TV, which can be indicated by the reconstructed shape and quantitative metrics. However, images generated by these two algorithms show evident change when SNR varies from 35 dB to 25 dB. In this case,
### 3.4. Results and Discussion

#### Figure 3.8: Comparison of the ability of voltage noise resistance.

<table>
<thead>
<tr>
<th>Noise Level</th>
<th>TReg</th>
<th>SA-SBL</th>
<th>EAGS-TV</th>
<th>IGGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNR=35 dB</td>
<td>0.9532</td>
<td>0.6279</td>
<td>0.4501</td>
<td>0.1333</td>
</tr>
<tr>
<td></td>
<td>0.2805</td>
<td>0.7970</td>
<td>0.8910</td>
<td>0.9661</td>
</tr>
<tr>
<td>SNR=25 dB</td>
<td>1.0253</td>
<td>0.6519</td>
<td>0.4752</td>
<td>0.1323</td>
</tr>
<tr>
<td></td>
<td>0.2545</td>
<td>0.6356</td>
<td>0.8860</td>
<td>0.9627</td>
</tr>
</tbody>
</table>

#### Figure 3.9: Image reconstruction results based on inaccurate mask image.

- **Mask Image**
- **Clean Voltage**
- **RIE MSSIM**

<table>
<thead>
<tr>
<th>SNR=35 dB</th>
<th>RIE</th>
<th>MSSIM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.2450</td>
<td>0.9732</td>
</tr>
<tr>
<td></td>
<td>0.2897</td>
<td>0.9663</td>
</tr>
<tr>
<td></td>
<td>0.3650</td>
<td>0.9527</td>
</tr>
</tbody>
</table>
3.4. Results and Discussion

Figure 3.10: Running time comparison. The values represent the running time (unit: second).

the images generated by TReg show unnoticeable degradation. Meanwhile, the results of IGGS also show a slight change when SNR decreases. The performance of IGGS presents the highest level compared with other algorithms, which indicates IGGS has the best noise resistance capability among these four given algorithms.

Fig. 3.9 selects phantom 3 to examine the noise-resistance ability of IGGS under noise-contaminated voltage data and inaccurate mask images. Two voltage noise levels, i.e. clean voltage data and voltage data with SNR=35 dB, are selected. In addition, the mask image suffers from three perturbation levels, i.e. accurate mask, slightly perturbed mask, and severely perturbed mask (from top to bottom). Inaccurate masks may be generated by the unideal semantic segmentation algorithms or caused by noisy guidance images in real scenarios. Therefore, investigation of the effect of inaccurate mask images is necessary for real applications. As Table V shows, the shape of objects in the reconstructed image is determined by the mask image. Given a fixed mask image, quantitative metrics are barely influenced by the voltage noise. While given a fixed voltage noise level, the metrics become worse when the mask image becomes inaccurate. However, the quantitative metrics of the results of IGGS are still superior to those images generated by the other three algorithms under the same voltage noise level. In addition, although given an inaccurate mask, the conductivity change can still be estimated relatively accurately except for the pixels at the boundary. This indicates IGGS has a good generalization ability when encountering inaccurate mask images. In summary, IGGS has a strong ability to resist voltage noise and mask perturbation.

The last comparison is concerned with the elapsed time. As the second and third steps of IGGS are fixed in practice and we don’t conduct semantic segmentation in simulation, we only compare the elapsed time of the second and third steps of IGGS with the other algorithms. The simulation data and algorithm parameter settings are the same as those in Fig. 3.6. The results are illustrated in Fig. 3.10. The image reconstruction is carried out on the MATLAB
3.4. Results and Discussion

Figure 3.11: Induced boundary voltage response of EIT. Linearization leads to the model error.

R2021a on a Windows laptop with an Intel® Core™ i7-10750 CPU. From Fig. 3.10, it is explicit that IGGS spends the minimum time for all phantoms, while TReg and SA-SBL are the two most time-consuming algorithms. Comparing IGGS with EAGS-TV, the less elapsed time is mainly benefited from the smaller number of iterations, indicating IGGS has the potential to be implemented for real-time image reconstruction in future applications.

Here we also present a brief discussion of the model error and its influences. In the adopted time-difference imaging model, the model error originates from the linearization of the non-linear problem of EIT. Specifically, the forward model of EIT, i.e. (2.6), is a non-linear mapping, while this paper adopts the commonly used linearized version, i.e. (2.8). Based on the linearized forward model, the EIT image reconstruction cannot recover accurate conductivity change distribution when the perturbation is not subtle. This is the primary reason that we normalize the reconstructed images and focus on the contrasts of the conductivity distribution. We qualitatively discuss the model error with the assistance of Fig. 3.11. In Fig. 3.11, we ignore all types of measurement error and confine the mapping from $\mathbb{R}$ to $\mathbb{R}$. Thus, the vector $\sigma$ and $V$ are simplified as the scalar $\sigma$ and scalar $V$, respectively. The blue curve represents the true EIT forward response and the orange straight line represents the linearized forward response. Note this simplification and the curves are just for illustration purposes. At the reference time point, the conductivity is denoted by $\sigma_0$ and the corresponding boundary voltage is represented by $V_0$. $V_1$ denotes the boundary voltage at the observation time point.
Based on the linear model and the voltage measurement $\Delta V = V_1 - V_0$, the reconstructed conductivity change is $\Delta \sigma = \sigma_1 - \sigma_0$. However, it should be $\sigma_1^* - \sigma_0^*$ according to the realistic non-linear model. Such deviation would affect the image reconstruction quality and accuracy in practical applications.

3.4.2 Real-world Experiments

The performance of IGGS is further validated on real-world data and the results are illustrated in Fig 3.12. The sensor is connected to the EIT system developed in the Intelligent Sensing, Analysis and Control Group (ISAC) at The University of Edinburgh and the highest Signal-to-Noise Ratio (SNR) of the system is 82.82 dB (Y. Yang & Jia, 2017b). As stated in Section III, we use two EIT sensors, i.e. EIT sensor A and EIT sensor B, to verify the proposed method. EIT sensor A is used to image square carrot tissues (length $\sim$ 3 mm) and the combination of a triangle rubber (large length $\sim$ 3 mm, small length $\sim$ 2 mm) and a hexagonal iron (diameter $\sim$ 3 mm). The Background medium for both phantoms is saline, which conductivity is 0.05 $\text{S/m}$. The upper surface of the iron is covered by a thin white rubber layer. The rubber layer does not affect the conductivity properties of this imaging target much, meanwhile, it can reduce surface reflection that may influence the definition of the object shape in the optical image. The EIT sensor B is employed to image MCF-7 cell spheroids (diameter $\sim$ 2 mm) which are cultured in PBS with a conductivity of 2 $\text{S/m}$. For all experiments, the current excitation frequency is set as 10 kHz and the current amplitude is set as 1.5 mA peak to peak. A completed frame contains 104 individual measurements, and the frame rate is 48 fps. The adjacent protocol is also adopted to collect boundary voltages (Brown & Seagar, 1987).

Based on the L-curve method (Hansen & O’Leary, 1993), the searched Tikhonov regularization factors for carrot tissues, the combination of a triangle rubber and a hexagonal iron, and MCF-7 cell spheroids are $2.5109 \times 10^{-5}$, $0.0015$ and $2.4612 \times 10^{-5}$, respectively. In addition, based on trials, the maximum iteration numbers are set as 100 and 40 for EAGS-TV and IGGS, for all experiments. In rubber and iron imaging, the penalty parameter for the $l_2$ norm related to auxiliary variable is set as $0.05/\text{mean(abs(}\Delta V\text{))}$ and the penalty parameter for the $l_2$ norm related to EIT linearized model is set as $10/\text{mean(abs(}\Delta V\text{))}$ for EAGS-TV. Other parameters for all algorithms and all experiments are set the same as those in the simulation study. In addition, the size of the structuring element is set as $3 \times 3$ for the two sets of segmentation algorithms throughout experiments. For the cell spheroid image segmentation, the value of $\tau$ is set as 0.45.

In Fig 3.12, mask images generated by the semantic segmentation algorithms are in the rightest column. We assume the mask images provide accurate geometrical distribution information and select them as the reference to calculate MSSIM for quantitative assessment of algorithm performance. For TReg and SA-SBL, the shape of imaging targets is deteriorated, and the images contain too much background noise although they can roughly locate the
3.4. Results and Discussion

Figure 3.12: Image reconstruction comparison based on experimental data.

position of imaging targets. EAGS-TV has a stronger capability of noise resistance compared to the former two methods, whereas it fails to reconstruct objects with accurate shapes. In contrast, only IGGS presents the best shape-preservation ability (see images and MSSIM) and background noise-resistance ability (see image background quality) for different types of miniature sensors and sensing objects.

3.5 Summary

This chapter proposed an EIT-optical dual-modal image reconstruction algorithm named IGGS to improve the image quality of EIT with the assistance of an extra imaging modality. IGGS fuses the dual-modal information from EIT and optical images to reconstruct high-quality EIT images. Both simulation studies and real-world experiments demonstrated that IGGS could generate more accurate contrasts of conductivity distribution than the comparative algorithms, implying the potential of performing impedance-based quantitative analysis for tissue engineering. Future work can extend the method to the three-dimensional imaging setup. Quantitative conductivity imaging based on the dual-modal setup can also be rigorously explored.
4.1 Introduction

Chapter 3 introduced an EIT-optical imaging framework along with the accompanying image reconstruction algorithm named IGGS for tissue engineering. The results demonstrated the effectiveness and high performance of the proposed method. However, the main drawback of IGGS is the necessity to segment the auxiliary image, which in turn introduces additional computational costs.

This chapter introduces an alternative approach to IGGS, namely the kernel method-based multi-modal EIT image reconstruction, designed to address the previously mentioned challenge. The kernel method enables segmentation-free information fusion at the image level and integrates the structural information of an auxiliary high-resolution image into the EIT inversion process through the kernel matrix. This integration gives rise to an unconstrained least square problem. We present this approach in a general manner, allowing high-resolution images from various imaging modalities to be adopted as auxiliary images if they contain sufficient structural information. In comparison to some state-of-the-art algorithms, the proposed kernel method produces superior EIT images in challenging simulation and experimental phantoms. It also offers the advantage of suppressing interference from imaging-irrelevant objects in the auxiliary image. Simulation and experimental results suggest that the kernel method holds great potential for application in more complex tissue engineering scenarios.
4.2 Kernel-based EIT Image Reconstruction

We introduce the kernel method to encode the structural information extracted from an auxiliary image obtained from a high-resolution imaging modality (e.g. CT, optical microscope, OCT) into EIT image reconstruction (see Fig. 4.1). This is inspired by the kernel-based image reconstruction methods investigated in PET image reconstruction, which have been proven effective in structure preservation (Hutchcroft, Wang, Chen, Catana, & Qi, 2016; G. Wang & Qi, 2014b). In this Section, we first describe the principle of EIT image reconstruction using kernel methods. Then, the practical definition of feature vectors, selection of kernels, and proximity criteria are stated. We also briefly introduce the comparing algorithms, i.e. standard Tikhonov regularization (TReg) (Vauhkonen et al., 1998) and Cross-Gradient regularization (Z. Li et al., 2019).

4.2.1 The Proposed Kernel-based Algorithm

We first predefine a set of low-dimensional feature vectors $f_i$ at each pixel $i$ in the expected EIT image. The set of feature vectors is the first of two mathematical objects which should be predefined in the kernel method framework (Hutchcroft et al., 2016; G. Wang & Qi, 2014b). The second mathematical object will be described later. After the feature vectors are defined, the conductivity change at pixel $i$, denoted by $\Delta \sigma_i$, can be expressed by the linear form:

$$\Delta \sigma_i = \phi^T (f_i)$$  \hspace{1cm} (4.1)
where, $\phi$ is a mapping which transforms $f_i$ into a very-high dimension space spanned by $\{\phi(f_j)\}_{j=1}^N$; $N$ is the number of pixels of the EIT image. $\varphi$ is a weight vector which sits in the same high-dimension space and is represented by:

$$\varphi = \sum_{j=1}^{N} \tau_j \phi(f_j)$$  \hspace{1cm} (4.2)

where $\tau_j$ is the coefficient for $\phi(f_j)$. Substituting (4.2) into (4.1), the conductivity change at pixel $i$ is written as:

$$\Delta\sigma_i = \sum_{j=1}^{N} \tau_j \phi(f_j)^T \phi(f_i) \triangleq \sum_{j=1}^{N} \tau_j \kappa(f_i, f_j)$$  \hspace{1cm} (4.3)

where $\kappa$ is a kernel that implicitly defines $\phi$. Therefore, $\phi$ is not required to be explicitly predefined. For simplicity, (4.3) can be expressed as the following matrix form:

$$\Delta\sigma = K\tau$$  \hspace{1cm} (4.4)

where the element of the kernel matrix $K$ at $(i, j)$ is $\kappa(f_i, f_j)$. Under the matrix form, each column of $K$ can be understood as a basis of $\Delta\sigma$ and $\Delta\sigma$ is the linear combination of all bases, i.e.

$$\Delta\sigma = \tau_1 K_{:,1} + \tau_2 K_{:,2} + \cdots + \tau_N K_{:,N}$$  \hspace{1cm} (4.5)

where, $K_{:,1}$ means the first column of $K$ and the meaning of other symbols are explained the same way. Many kernels, such as polynomial kernel, can be selected to build the kernel representation of $\Delta\sigma$. Thus, the kernel is the second mathematical object which should be predefined. It should be emphasized that the construction of the kernel matrix is based on the predefined feature vectors and the kernel function. Therefore, $K$ is exactly the interface through which we can incorporate certain prior information into EIT image reconstruction.

In practical implementation, the full version of $K$ for an image is usually very large, resulting in low-computational efficiency. To address this issue, the full kernel matrix $K$ is replaced by a sparse version $K^S$ in this work. The element of $K^S$ at $(i, j)$ is:

$$K^S_{i,j} = \begin{cases} 
\kappa(f_i, f_j), & j \in kNN \text{ of } i \\
0, & \text{otherwise}
\end{cases}$$  \hspace{1cm} (4.6)

where, $kNN$ is the $k$ nearest neighbors of the pixel $i$ in a $d \times d$ window centered at it (named as the search window) and $d$ should be predefined. This approach is similar to the method adopted in the non-local mean filtering to improve computational efficiency. The search of the similar window is conducted on the size-predefined search window rather than the entire
4.2. Kernel-based EIT Image Reconstruction

image (Buades, Coll, & Morel, 2005). In addition, in Section IV, we will demonstrate that the sparse kernel matrix is more suitable for EIT image reconstruction under our settings than the full version. During the process of $K^S$ calculation, the degree of proximity between two pixels should also be judged by a predefined proximity criterion.

Finally, substituting the equation $\Delta \sigma = K^S \tau$ into (2.10) and discarding the regularization term in (2.10), the coefficient vector $\tau$ can be estimated by:

$$\hat{\tau} = \arg \min \tau \frac{1}{2} ||SK^S \tau - \Delta V||^2,$$

where $S$ is equal to $J$ in (2.10).

The solution of (4.7) naturally leads to the ultimately estimated EIT image $\hat{\sigma}$:

$$\hat{\sigma} = K^S \hat{\tau}.$$

Equation (4.7) is a standard unconstrained least-squares problem that can be effectively solved by the simple gradient descent method. The iteration equation for solving (4.7) is:

$$\tau_{t+1} = \tau_t - \alpha (K^S)^T S^T (SK^S \tau_t - \Delta V)$$

where, $t$ represents iteration step and $\alpha$ denotes the iteration step length. We adopt early stopping as a stopping criterion for our kernel-based algorithm.

4.2.2 Feature Definition, Kernel Selection, Proximity Criteria, and Other Implementation Details

In this study, we let the size of the auxiliary image equal to that of the EIT image. Thus, auxiliary image pixels and EIT image pixels coincide. Elements of the feature vector $f_i$ are defined as the intensity values of pixels in the $y \times y$ window centered at pixel $i$ in the auxiliary high-resolution image. This window is called the feature window and $y$ should also be predefined. How to rearrange the elements of a feature window into a vector is illustrated in Fig. 4.1. The widely used radial Gaussian kernel is adopted, which is defined as:

$$\kappa(f_i, f_j) = \exp \left(-\frac{||f_i - f_j||^2}{\varepsilon^2}\right),$$

where $\varepsilon$ controls the sensitivity to the boundary. The $kNN$ of the pixel $i$ are in its search window and Euclidean distances between feature vectors of $kNN$ and $f_i$ are the $k$ shortest distances among all pixels in this search window. This type of $kNN$ selection method is exactly the proximity criteria.
The relationship of \( k \) and \( d \) should satisfy \( k \leq d^2 \). Usually, we define \( d \) and \( y \) as the odd number and let \( y < d \). Before \( K_S \) calculation, the feature vectors \( \{f_i\}_{i=1}^N \) are normalized by the following equation:

\[
\bar{f}_{i,z} = \frac{f_{i,z}}{\text{std}_z(f)}
\]

where, \( f_{i,z} \) is the \( z^{th} \) element of \( f_i \), and \( \text{std}_z(f) \) is the standard deviation of \( z^{th} \) elements of all feature vectors. Furthermore, \( K_S \) is row-normalized after its construction.

It is noteworthy that the kernel matrix \( K_S \) is calculated based on the auxiliary high-resolution image. Thus, \( K_S \) can be considered the container storing encoded information offered by the auxiliary image, which is exactly how the structural information of the auxiliary image is associated with EIT image reconstruction.

For pixels at or near the boundary of the auxiliary image, if part of the search window of a pixel is out of the image region, pixels, where the image region intersects with the feature window, are set as the \( kNN \) candidates. Furthermore, the number of \( kNN \) may exceed the number of \( kNN \) candidates. In this case, all \( kNN \) candidates will be set as \( kNN \). Likewise, at or near the boundary, part of the feature window of a pixel may be out of the image region. We apply zero padding to the auxiliary image to deal with this situation.

### 4.2.3 Standard Tikhonov Regularization and Cross-Gradient Regularization

We implemented standard Tikhonov regularization (TReg) (Vauhkonen et al., 1998) and Cross-Gradient regularization (Z. Li et al., 2019) for comparison. The reasons for choosing TReg are twofold. First, it is the most basic algorithm in EIT image reconstruction and can be considered the baseline of other algorithms. Second, it is the basis for the Cross-Gradient method, which can be reflected by (4.12) and (4.13). Compared with the estimated EIT image by TReg, one can easily find the change in the EIT image when incorporating the Cross-Gradient regularization term. The Cross-Gradient method incorporates structural information of the auxiliary image through a penalty term, which is a different regularization approach from our method. The definitions of TReg and Cross-Gradient method are expressed by (4.12) and (4.13) respectively:

\[
\hat{\Delta}\sigma = \arg\min_{\Delta\sigma} \frac{1}{2} \| S\Delta\sigma - \Delta V \|^2 + \frac{1}{2} \| \lambda E\Delta\sigma \|^2
\]

\[
\hat{\Delta}\sigma = \arg\min_{\Delta\sigma} \frac{1}{2} \| S\Delta\sigma - \Delta V \|^2 + \frac{1}{2} \| \lambda E\Delta\sigma \|^2 + \frac{1}{2} \| \gamma G(\Delta\sigma, \phi) \|^2
\]

where \( \delta \) denotes the identity matrix. \( \lambda \geq 0 \) is the Tikhonov regularization coefficient and \( \gamma \geq 0 \) is the Cross-Gradient coefficient. \( G(\Delta\sigma, \phi) \) represents the Cross-Gradient vector between the conductivity change \( \Delta\sigma \) and the pixel values of the auxiliary image \( \phi \). \( G(\Delta\sigma, \phi) \) can be expressed as a matrix form of \( G(\Delta\sigma, \phi) = G_\phi \Delta\sigma \); \( G_\phi \) is the transformation matrix related to \( \phi \). Thus, both (4.12) and (4.13) can be rewritten as the form of standard least squares, (4.14)
4.2. Kernel-based EIT Image Reconstruction

Figure 4.2: Modelled (a) EIT sensor, (b) phantom 1, (c) phantom 2, (d) noiseless auxiliary image for phantom 1 and (e) noiseless auxiliary image for phantom 2.

and (4.15), respectively:

\[
\hat{\sigma} = \arg\min_{\sigma} \frac{1}{2} \left\| \begin{bmatrix} S \\ \lambda E \end{bmatrix} \sigma - \begin{bmatrix} \Delta V \\ 0 \end{bmatrix} \right\| ^2
\]

\[
\hat{\sigma} = \arg\min_{\sigma} \frac{1}{2} \left\| \begin{bmatrix} S \\ \lambda E \gamma G \phi \end{bmatrix} \sigma - \begin{bmatrix} \Delta V \\ 0 \end{bmatrix} \right\| ^2
\]

Therefore, the TReg and Cross-Gradient regularization-based algorithms can also be solved by the same gradient descent method, further improving comparison fairness. Since SA-SBL is developed from another inverse framework, i.e., the Bayesian perspective, it is interesting to select it to compare.

4.3 Results and Discussion

We evaluate the effectiveness and robustness of the proposed kernel method on several challenging numerical and experimental phantoms involving complex structures, i.e., straight lines, angles and curves, and noisy auxiliary images. The quantitative metrics used in this section are RIE and MSSIM, which are defined in (3.27) and (3.28), respectively.

4.3.1 Synthetic Data Evaluation

Modelling

We modelled an EIT sensor in COMSOL Multiphysics as illustrated in Fig. 4.2 (a). The sensing area is circular, and its diameter is set as 15 mm. The homogeneous saline with a conductivity value of 0.05 S/m is set as the background or reference medium for time difference imaging. Sixteen electrodes are evenly attached on the outer surface of the sensing area,
and the electrode material is selected as Titanium whose conductivity is $7.407 \times 10^5 \, \text{S/m}^{-1}$.

In addition, we modelled two types of complex conductivity distribution, i.e., phantom 1 to phantom 2 (see Fig. 4.2 (b) and Fig. 4.2 (c)). Phantom 1 simulates two objects. The upper right is a triangle with a conductivity value of $0.08 \, \text{S/m}^{-1}$, and the bottom left is a rectangle with a conductivity value of $0.035 \, \text{S/m}^{-1}$. Phantom 2 simulates three dispersed objects, including a ring with a conductivity value of $0.035 \, \text{S/m}^{-1}$ (bottom left), a circle with a conductivity value of $0.015 \, \text{S/m}^{-1}$ (upper left), and an ellipse with a conductivity value of $0.025 \, \text{S/m}^{-1}$ (right) respectively. The adjacent sensing protocol (Brown & Seagar, 1987) is adopted in simulation, and a frame of voltage data consists of 104 measurements (Geselowitz, 1971). In addition to noiseless voltage data, two levels of Gaussian noise-contaminated voltage data are also used, i.e., voltage data with SNR = 50 dB and SNR = 20 dB. The below equation defines the SNR:

$$SNR \triangleq 10 \log_{10} \left( \frac{\| \Delta V \|^2}{E(\| \mathcal{N} \|^2)} \right)$$  \hspace{1cm} (4.16)

where $\mathcal{N} \in \mathbb{R}^M$ is the random noise variable; $E(\cdot)$ is the mapping of expectation. For dual-modal algorithms, i.e., Cross-Gradient and kernel method, assisted images should also be modeled. We makes the size of the auxiliary image the same as that of the EIT image. In addition, we assume the auxiliary image provides accurate structure information. In real applications, these images can be collected from CT imaging or optical imaging. In the simulation, they are generated by assigning digit one to pixels corresponding to imaging targets and assigning digit 0.5 to the background pixels. The noiseless auxiliary images of samples 1 and 2 are shown in Fig. 4.2 (d) and Fig. 4.2 (e), respectively.

**Parameter Settings**

In simulation study, for each algorithm, different phantoms may take different parameters for better results. If not specified, all parameters use the following settings in the simulation study. For both phantoms using SA-SBL, the maximum iteration number is set as 5; the tolerance is selected as $1 \times 10^{-5}$ and the block size is fixed as 4. The pattern coupling factor takes different values for the two phantoms, and it is chosen as 0.03 for phantom 1 and is set as 0.5 for phantom 2. According to trials, $\lambda$ for both Tikhonov and Cross-Gradient regularization is set as 0.01 for all cases and $\gamma$ for Cross-Gradient regularization is set as 0.1 for all cases. For Cross-Gradient regularization, the iteration number is set as 3000, and the iteration step length is 5 for all cases. For the kernel method, the iteration number is selected as 1000 and the step length is set as 10; $\gamma$ is set as 3; $d$ is set as 21; $k$ is set as 441; and $e^2$ is set as 20 for both phantoms.
Reconstruction Results and Discussion

Fig. 4.3 compares the performance of the kernel method with Tikhonov, Cross-Gradient regularization, and SA-SBL with SNR = 50 dB data and noiseless auxiliary images. The TReg can predict the position of imaging targets correctly, but the structure information of targets is vague from the visualized images and MSSIM. Additionally, the accuracy of conductivity prediction is very low (see its RIE). The Cross-Gradient can provide some structural information evident in the zoomed part of images of phantom 1, i.e., straight lines of the square object can be seen. In addition, the shape of the triangle object can also be identified. However, the Cross-Gradient regularization is not sensitive to circular boundaries (see phantom 2 results). Our results also indicate that the image quality generated by Cross-Gradient highly relies on the image quality generated by Tikhonov regularization, which is also indicated in the original paper (Vauhkonen et al., 1998). The Cross-Gradient regularization can only slightly adjust the object shape but cannot effectively fuse structural information and cannot improve the accuracy of conductivity contrast estimation. The SA-SBL recovers some object shapes well, such as the triangle object in phantom 1. However, most of the structural information is still lost. Though, the shape recovery of SBL is much worse than the kernel method through visualization, the MSSIM of SA-SBL is larger than that of the kernel method for phantom 1. The same occurs when we set the pattern coupling factor of SA-SBL as 0.03 for phantom 2, which leads the MSSIM of SA-SBL to 0.8328. This is because, in the given phantoms, the background values are more dominant when calculating MSSIM. Since sparsity regularization is used in SA-SBL, it makes the background values of the images generated by SA-SBL closer to zeros than those based on the kernel method. Since the ring object is almost invisible in the image generated by SA-SBL for phantom 2 based on the pattern coupling factor of 0.03, we show the results based on such parameter of 0.5. In the former case, the RIE is 0.6973 and MSSIM is 0.8326. Therefore, we can conclude that the proposed kernel method can predict EIT images with the most accurate position, structure, and conductivity contrasts.

Fig. 4.4 displays results under a considerably challenging situation, i.e., we selected phantom 1 to test the robustness of the kernel method under noise-contaminated voltage data and noise-contaminated auxiliary image. We added three types of noise to the auxiliary image, i.e., Gaussian noise, Speckle noise, and Salt and Pepper noise. The mean and variance of the Gaussian noise are set as zero and 0.01. The Speckle noise is based on the following equation:

\[ III^* (h, b) = III (h, b) + t (h, b) \odot III (h, b), \]  

(4.17)

where \( III^* \) is the noisy image and \( III \) is the noiseless image. \( t \) represents uniformly distributed random noise with mean zero and variance 0.05. \( \odot \) represents Hadamard product. The Salt and Pepper noise is added with the noise density of 0.1, which means the noise will affect approximately 10% of all pixels. As shown in Fig. 4.4, given a specific auxiliary image, the kernel method shows a good voltage noise resistance capability (see RIE, MSSIM and EIT.
4.3. Results and Discussion

Figure 4.3: Image reconstruction comparison based on simulation data.

Images). Especially, the object shape is slightly affected by the voltage noise. Given a specific voltage data, the results show that the Salt and Pepper noise can degrade the reconstructed image quality most and the Gaussian noise has the minimal adverse impact on the image quality. All types of image noise do not influence the object shape much. The kernel method demonstrates satisfactory voltage noise resistance and assisted image noise resistance.

Subsection 4.2.1 mentions that columns of the kernel matrix can be considered as the basis for the EIT image. In other words, the EIT image can be regarded as the linear combination of all bases. Here, we try to explain how this combination works in a visualized way. We display four columns of the sparse kernel matrix calculated in the noiseless-assisted image based on phantom 2. As shown in Fig. 4.5, each column represents a sub-image of the ultimate EIT image, and each sub-image highlights different part of the ultimate EIT image. For example, the 848th column highlights conductivity in the bottom left area. As pixels in the ring have different structures than its peripheral region, it is not highlighted in this case. Therefore, the coefficient vector is the weights that define each sub-image’s significance in the ultimate EIT
4.3. Results and Discussion

| Table 4.4: Assessment of auxiliary image noise and voltage noise resistance ability for kernel method. |

<table>
<thead>
<tr>
<th>Assisted Image</th>
<th>50 dB</th>
<th>20 dB</th>
<th>Assisted Image</th>
<th>50 dB</th>
<th>20 dB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noiseless</td>
<td>0.3955</td>
<td>0.5997</td>
<td>Gauss</td>
<td>0.4270</td>
<td>0.4398</td>
</tr>
<tr>
<td>RIE</td>
<td>0.7822</td>
<td>0.7044</td>
<td>RIE</td>
<td>0.7542</td>
<td>0.6641</td>
</tr>
<tr>
<td>MSSIM</td>
<td></td>
<td></td>
<td>MSSIM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Speckle</td>
<td>0.4530</td>
<td>0.4751</td>
<td>Salt and Pepper</td>
<td>0.4914</td>
<td>0.5014</td>
</tr>
<tr>
<td>RIE</td>
<td>0.7247</td>
<td>0.6427</td>
<td>RIE</td>
<td>0.6230</td>
<td>0.5210</td>
</tr>
<tr>
<td>MSSIM</td>
<td></td>
<td></td>
<td>MSSIM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 4.4: Assessment of auxiliary image noise and voltage noise resistance ability for kernel method.

Figure 4.5: Visualized images of columns in sparse kernel matrix: (a) column 10, (b) column 705, (c) column 848, and (d) column 2400.

image. As non-zero regions (non-blue regions) in different sub-images may overlap and all sub-images will finally be added together with weights, this can reduce the influence of the noise in the assisted image to some extent. Fig. 4.5 also provides a qualitative explanation regarding why the kernel method shows auxiliary image noise resistance.

In Fig. 4.6, we discuss the influence of parameters $k$, $\varepsilon^2$, $d$, and $\gamma$. For all analyses in this figure, the iteration number and iteration step length are fixed as 1000 and 10, respectively. We set $\gamma$ equal 3, $d$ equal to 21 and $\varepsilon^2$ equal to 20 to analyze the influence of $k$. The results are shown in Fig. 4.6 (a), which indicates the MSSIM will be better if $k$ increases while the RIE has a decreasing trend. Although RIE based on phantom 2 increases when $k$ is very large, the increment is also acceptable. Therefore, we can always choose $k$ equal to or close to the number of pixels of the search window. We set $\gamma$ equal 3, $d$ equal to 21 and $k$ equal to 441 to analyze the influence of $\varepsilon^2$, and the results are illustrated in Fig. 4.6 (b). Fig. 4.6 (b) presents that there is a window for the selection of $\varepsilon^2$, which indicates that the best range for $\varepsilon^2$ is around 5-50. We recommend finetuning this parameter based on specific applications.
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![Graphs showing parameter analysis](image)

**Figure 4.6:** Parameter analysis: analysis of the influence of (a) $k$, (b) $\varepsilon^2$, (c) $d$, and (d) $y$. RIE1 and MSSIM1 are the RIE and MSSIM for phantom 1. RIE2 and MSSIM2 represent the RIE and MSSIM for phantom 2. The two metrics share the same vertical coordinate.

To discuss the influence of $d$, we fix $y$ as 3, $\varepsilon^2$ as 20 and all pixels in the search window as the $kNN$. The results in Fig. 4.6 (c) demonstrate that $d$ should not be too small or too large. It should be noted in Fig. 4.6 (c) that if $d$ is much larger, such as 61, the MSSIM decreases significantly for phantom 1 due to the insufficient iteration number. Thus, we also study the influence of the iteration number (up to 8000) based on different $d$. As shown in Fig. 4.7, we can conclude that if given a large enough search window ($d \geq 21$), the MSSIM will converge to a satisfactory value. Though MSSIM-81 and MSSIM-whole in Fig. 4.7 (b) are still a little small at the 8000th iteration, they also have the trend of increasing. However, the RIEs based on phantom 1 (see Fig. 4.7 (a)) converge while RIEs based on phantom 2 increase (see Fig. 4.7 (b)) with the increase of the iteration number. If the search window size is not too large, such as 21, the increment of RIEs based on phantom 2 is a little. Combining the results of Fig. 4.6 (c) and Fig. 4.7, it is easy to find that large $d$ will positively impact MSSIM while deteriorating...
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Figure 4.7: Analysis of the influence of $d$ based on (a) phantom 1 and (b) phantom 2. Numbers in legends mean the side length of the search window, and ‘whole’ means the kernel matrix is calculated based on the entire image.

Figure 4.8: Image reconstruction results based on unreasonable $\varepsilon^2$. (a) and (c) are the reconstructed images based on $\varepsilon^2 = 1$ and $\varepsilon^2 = 1000$, respectively. (b) and (d) are the visualizations of the 848th column of the sparse kernel matrix corresponding to (a) and (c), respectively.

the RIE. Therefore, the size of the search window should be carefully selected. In our study, $d$ equal to 21 always generates satisfactory results. Fig. 4.6 (d) analyzes the influence of $y$. In this case, we set $d$ as 21, $kNN$ as 441 and $\varepsilon^2$ as 20. From this figure, it is obvious that the size of the feature window should not be set too large due to the small size of the reconstructed EIT image. Otherwise, local information will be deteriorated due to the large feature window size. Therefore, $3 \times 3$ is recommended for the feature window size. According to the analysis, though the number of kernel method parameters, i.e., $y$, $d$, $k$, $\varepsilon^2$, seems to be large, only $\varepsilon^2$ should be carefully selected.

To further highlight the importance of the $\varepsilon^2$ selection, in Fig. 4.8, we show the reconstruction results of phantom 2 by using the kernel method with unreasonable $\varepsilon^2$. Other parameters are the same as those in Parameter Settings of the Subsection 4.3.1. The SNR is 50 dB and noise-free auxiliary image is adopted. Fig. 4.8 (a) is the reconstructed image based on the $\varepsilon^2$ of 1 and Fig. 4.8 (c) is the reconstructed image based on the $\varepsilon^2$ of 1000. For each
4.3. Results and Discussion

Figure 4.9: Image reconstruction results of the phantom 1 based on incorrect auxiliary images. (a) is the auxiliary image corresponding to the reconstructed image (b). (c) is the reconstructed image adopting the auxiliary image in Fig. 4.2 (e).

situation, the 848th column of the sparse kernel matrix (Fig. 4.8 (b) and Fig. 4.8 (d)) is also displayed, and it stands for why the image quality is low. Small $\varepsilon^2$, e.g. $\varepsilon^2 = 1$, is sensitive to the edge; thus, the sparse kernel matrix overextracts the structure. Contrarily, large $\varepsilon^2$, like $\varepsilon^2 = 1000$, treats each pixel in the highlighted area of the auxiliary image the same, making the sparse kernel matrix lack structural information. Therefore, selecting a reasonable $\varepsilon^2$ is vital in practice.

It is worth discussing the scenario of the wrong auxiliary image being adopted when using the kernel method though this can be rare in practice. We select phantom 1 to demonstrate the effect. The voltage data of phantom 1 is contaminated with noise (SNR = 50 dB), and the parameters for the kernel method follow the settings in Section IV-A-2). The reconstructed images in Fig. 4.9 (b) and Fig. 4.9 (c) are based on the auxiliary images in Fig. 4.9 (a) and Fig. 4.2 (e), respectively. It is noted that the reconstructed images are very chaotic. Though these images can still indicate conductivity and structural information of the auxiliary image to a certain extent, the whole image is entirely incorrect. The RIE and MSSIM figures can also indicate this. In summary, the voltage data and the auxiliary image should match when using the kernel method.

Lastly, we choose phantom 2 to study the value change of the objective function (or loss function) of the optimization problem (4.7) with the iteration number. The result is illustrated in Fig. 4.10. This figure demonstrates that we can increase the iteration step length to make convergence faster. In addition, as the loss decreases smoothly, this also provides evidence for the reliability of the early stopping criteria for our algorithm.
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Figure 4.10: Changes of the objective function (loss function) in (4.7) with the increasing of iteration number based on different iteration step lengths (SL) and phantom 2. In legend, numbers mean the selected iteration numbers discussed.

Figure 4.11: (a) Side view of manufactured EIT sensor, (b) top view of manufactured EIT sensor, and (c) in-house built EIT system.
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4.3.2 Experimental Data Evaluation

In this Subsection, the performance of the kernel method is further validated on real experimental data. The adopted miniature EIT sensor is illustrated in Fig. 4.11, and it is connected to the EIT system developed in the Agile Tomography Group at The University of Edinburgh (Y. Yang & Jia, 2017b). The EIT sensor is used to image four different conductivity phantoms, and the results are illustrated in Fig. 4.12. The background medium for all cases is saline which conductivity is 0.05 S/m. Fig. 4.12 (a) and (b) are results of carrot tissue (length ∼ 3 mm) imaging. Fig. 4.12 (c) corresponds to rubber (bottom, large side length ∼ 3 mm, short side length ∼ 1.5 mm) and carrot tissue (upper right, large side length ∼ 3.5 mm, short side length ∼ 2 mm) imaging. Fig. 4.12 (d) demonstrates the results of the imaging on rubber (left, diameter ∼ 1.5 mm), iron (bottom, diameter ∼ 2 mm), and ginger tissue (top, side length ∼ 2 mm). The top surface of the iron is coated with a thin layer of white rubber to reduce the influence of surface reflection while preserving its electrical properties.

The auxiliary images for Cross-Gradient and kernel methods were collected from a digital camera placed over the EIT sensor. We adopted two types of auxiliary grey-scale images for each conductivity imaging, which are shown in Fig. 4.12. These images are circular images inscribed in the 704 × 704 square region. Therefore, they cannot be directly used to construct the sparse kernel matrix. We down-sampled them to the EIT image size before feeding them into the kernel-based algorithm. For visualization purposes, we display the non-down-sampled auxiliary images in Fig. 4.12.

To generate the non-down-sampled auxiliary image for each phantom, we firstly recorded an RGB microscopic image without objects as the calibration image represented by $I^c$. Then, an RGB microscopic image containing imaging targets is recorded and it is denoted by $I^o$. Due to the measurement error, we properly cropped the recorded $I^o$ and $I^c$ to make the imaging targets as close to the correct position as possible, which may cause the electrodes not to be evenly distributed along the circular boundary in the auxiliary image. Finally, the first type of auxiliary image (upper auxiliary image for each phantom) is generated by converting $I^o - I^c$ to a grey-scale image, and the second type of auxiliary image (bottom auxiliary image for each phantom) is generated by directly transforming $I^o$ to a grey-scale image.

Parameter settings for experimental data are based on a series of trials. For SA-SBL, the pattern coupling factor takes 0.03 for all phantoms, and other parameters are the same as those in Parameter Settings of the Subsection 4.3.1. For TReg and Cross-Gradient, the iteration number and iteration step length are 500 and 2, respectively. $\lambda$ for both TReg and Cross-Gradient is set as 0.01 and $\gamma$ for Cross-Gradient is selected as 1 for all cases. Except for the iteration number for phantom 1 and $\epsilon^2$ for phantom 4, parameters of the kernel method take the same settings as those in Parameter Settings of the Subsection 4.3.1. The iteration number for phantom 1 is set as 500 for two cases. $\epsilon^2$ is set as 15 for the upper auxiliary image of phantom 4 and it is chosen as 7 for the bottom auxiliary image of phantom 4.
To quantitatively compare the reconstruction results and highlight the phantom structure in the auxiliary image, we convert the first type of auxiliary images of all phantoms into its binary version, which will be used as the reference image for MSSIM calculation. We first normalize the auxiliary image and use the simple thresholding method to segment the auxiliary image. Pixel values lower than the threshold are set as zero, and those larger than the threshold are.
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set as one. The threshold values are selected based on trial and error, and they are 0.4, 0.4, 0.4 and 0.5 for phantom 1, 2, 3 and 4, respectively. Then open operation (Gonzales & Wintz, 1987) is applied to the segmented image to adjust the boundary of the objects. The size of the structuring element is chosen as $3 \times 3$ as we cannot make a significant change to the object boundary.

The image reconstruction results are illustrated in Fig. 4.12. In miniature-scale EIT imaging, the addition of imaging targets to the chamber will considerably vary the height of the background medium. This means the reference conductivity changes, which will cause severe artifacts in the reconstruction images based on all algorithms. For TReg, the shape of imaging targets deteriorates. The image quality is also much lower for Cross-Gradient. The results are however reasonable. In addition to the significant impact of the liquid height change and voltage noise, the auxiliary images also contain noise and imaging-irrelevant objects (e.g., electrodes) for EIT imaging. In addition, as discussed in Reconstruction Results and Discussion of the Subsection 4.3.1, the low image quality generated by TReg can be considered another reason that underlies the worst results of the Cross-Gradient method. The SA-SBL is also powerless under this challenging experimental setup. Only the proposed kernel method presents the best performance in terms of shape preservation. Besides, it can also recover the conductivity contrasts of different objects. For example, in imaging ginger, rubber, and iron, the conductivity of rubber is much lower than the ginger, and the iron introduces a positive conductivity change. The kernel method can differentiate the three different conductivity levels.

Furthermore, it is impressive that this method can suppress the adverse effect of imaging-irrelevant objects (e.g., electrodes) in the auxiliary image, which is indicated by the background quality of the reconstructed EIT image. For all cases, though the images of SA-SBL are chaotic, MSSIM values of SA-SBL are larger than those of the kernel method. This is because the background value dominates the MSSIM value. As sparsity regularization is used in SA-SBL, its background tends to be zero. Taking this into account, we can conclude the kernel method achieves the best performance on the challenging experimental data among given algorithms. To further validate this claim, we also use the thresholding method to extract the imaging targets. For each phantom, the two reconstructed images based on different auxiliary images take the same threshold value. For phantom 1 ~ 3, pixel values larger than the threshold are set as zero. The threshold values are also selected based on trials, and they are $-0.2, -0.2, \text{ and } -0.3$ for phantom 1, 2, and 3, respectively. For phantom 4, the absolute values of the pixels lower than 0.22 are set as zero. The segmentation results are illustrated in Fig. 4.13. The numbers in this table are the MSSIM values. It is verified that the background noise and artifacts cause the low MSSIM in Fig. 4.12 for the kernel method.
4.4 Summary

This chapter proposed a kernel-based method for dual-modal EIT image reconstruction. The robustness and effectiveness of this method are verified by numerical simulation and real-world experiments. In particular, the effectiveness of the kernel method can be explained in a visualized way, which is straightforward and provides evidence of reliability when applying this method in real applications. Future research will investigate the performance of different kernel functions for multi-modal EIT image reconstruction. In addition, the kernel method will be extended to 3D EIT image reconstruction and combined with other imaging modalities, e.g., OCT, to explore quantitative monitoring of 3D cultivated cells and tissues.
5.1 Introduction

Chapters 3 and 4 introduced two multi-modal model-based algorithms, namely IGGS and the Kernel Method, respectively. Each of these approaches has its limitations. Specifically, IGGS requires an additional segmentation algorithm to assist in pixel grouping, and it relies on carefully designed grouping rules. The Kernel Method demonstrates a performance that can be described as average in suppressing background artifacts. In order to address these limitations, this chapter presents a segmentation-free dual-modal EIT image reconstruction algorithm that employs Overlapping Group Lasso and Laplacian (OGLL) regularization. OGLL combines the strengths of both IGGS and the Kernel Method. Similar to IGGS, OGLL incorporates the structural information of the auxiliary image into EIT inversion through group lasso regularization. However, OGLL differs in its approach by utilizing overlapping groups and grouping conductivity changes based on local characteristics of the auxiliary image, drawing inspiration from the Kernel Method. The contributions of this Chapter are summarized as:

• This work first incorporates the overlapping group lasso into dual-modal EIT image reconstruction. OGLL demonstrates considerable improvements in structure preservation, background artifact suppression, and differentiation of conductivity contrasts compared with other single-modal and multi-modal image reconstruction algorithms.

• OGLL introduces a new grouping method, which is regular and controllable, leading to stable grouping results. As OGLL allows group overlapping, the requirement of fine-designed grouping rules and certain prior information (e.g., the number of groups) for non-overlapping grouping is unnecessary.

• The Laplacian regularization in OGLL can alleviate the artifacts caused by group overlapping (abbreviated as GOA). It enables flexible grouping strategies for OGLL, i.e., using the search window with various sizes and step lengths.
5.2 EIT Inverse Problem Based on Normalized Linear Forward Model

We adopt the time-difference imaging approach and describe the inverse problem in this specific setup. The mesh adopted for the circular sensing region is illustrated in Fig. 5.1 (a). The normalized linear forward model considered in this study is described by:

\[
V = J\sigma,
\]

(5.1)

where \(V = \frac{V_o - V_r}{V_r}\) and \(\sigma = \frac{\sigma_o - \sigma_r}{\sigma_r}\). \(V_o \in \mathbb{R}^M\) and \(V_r \in \mathbb{R}^M\) represent the measured voltages at the observation and reference time points. \(\sigma_o \in \mathbb{R}^N\) and \(\sigma_r \in \mathbb{R}^N\) account for the conductivity distribution at the observation and reference time points, respectively. At the reference time point, the conductivity distribution is homogeneous. \(N\) is the number of pixels of the EIT image and \(M\) is the number of measurements. Vector division means element-wise division. In this Chapter, \(J \in \mathbb{R}^{M \times N}\) denotes the normalised sensitivity matrix (Z. Liu, Gu, Chen, Bagnaninchi, & Yang, 2023). This matrix differs from the ordinary sensitivity matrix in (2.8). Similarly, \(V\) and \(\sigma\) are referred to as normalised voltage change and normalised conductivity change, which are also distinct from those in (2.6) (Z. Liu et al., 2023).

The general approach to formulate the inverse problem of EIT, which estimates \(\sigma\) subject to the (5.1), is expressed by:

\[
\min_{\sigma} R(\sigma)
\quad \text{s.t. } J\sigma = V,
\]

(5.2)

where \(R : \mathbb{R}^n \to \mathbb{R}\) denotes the regularization function, which encodes the prior information.

5.3 Image Reconstruction based on OGLL

OGLL comprises two steps, i.e., conductivity grouping and image reconstruction. Conductivity grouping is the key to constructing the group lasso regularization term. The idea of using group lasso encoding the prior information is based on the observation that, in biomedical applications, the EIT image usually shows local similarity for biological tissues with similar function or anatomy. Specifically, in time-difference imaging, the zero changes of the conductivity and non-zero akin changes of the conductivity typically present the property of local clustering. In addition, the group lasso can promote sparsity on the group level and discourage sparsity within each group (Huang & Zhang, 2010). Therefore, grouping similar conductivity changes can mitigate the ill-posedness of the EIT inversion and improve reversibility. For the image reconstruction step, OGLL solves the optimization problem using the Alternating Direction Method of Multipliers (ADMM) (Boyd et al., 2011). More details of OGLL are as follows.
5.3. Image Reconstruction based on OGLL

Figure 5.1: Illustration of EIT inverse mesh and overlapping groups. (a) is the mesh for the EIT inverse problem which consists of 3228 simplexes. (b) ~ (d) shows a grouping example. (b) is an example with one inclusion which is indicated by blue simplexes in (b) and (c). In (c), the colored square boundary defines the search window and the colored region means grouped pixels. Different colors represent different groups. Fuchsia circular disks denote all centers of search windows in the first grouping stage. In (d), light purple region shows grouped pixels (may belong to different groups) in the first grouping stage. The remaining pixels are ungrouped. Green circular disks stand for centers of search windows and blue square boundary represents the search window in the second grouping stage. Blue arrows in (c) and (d) indicate the moving direction of the search window.

5.3.1 Conductivity Grouping

In OGLL, conductivity grouping is based on the pixel similarity over the auxiliary image. To avoid ambiguity, we strictly impose that the size of the auxiliary image is the same as that of the EIT image. A pixel at the same position in both the EIT and auxiliary images corresponds to the same point of the imaging target. Usually, images generated by the auxiliary modality like CT are larger than EIT images, and the auxiliary images are acquired by down-sampling them into the EIT image size.

Before grouping, we predefine a set of feature vectors \( \{f_n \in \mathbb{R}^W, W \geq 1\}_{n=1}^N \) to characterize the pixels of the EIT image and a measure function \( \iota: \mathbb{R}^W \times \mathbb{R}^W \rightarrow \mathbb{R} \) to evaluate the similarity between different pixels of the EIT image. In general, \( f_n \) and \( \iota \) are selected based on the characteristics of the auxiliary image. For example, intensity values of the \( 3 \times 3 \) window centered at the \( n^{\text{th}} \) pixel of the auxiliary image can form the 9-element feature vector for the \( n^{\text{th}} \) pixel of the EIT image. In this study, \( f_n \) is defined as the \( n^{\text{th}} \) pixel intensity of the auxiliary image, and the below exponential function is selected as the similarity measure:

\[
\iota(f_n, f_k) = \exp\left(-||f_n - f_k||^2\right),
\]

(5.3)

where \( || \cdot || \) denotes the \( l_2 \) norm. We define that two elements of \( \sigma \) belong to the same group if \( \iota \) of their feature vectors is larger than a pre-defined positive threshold \( \phi \).
The grouping process is composed of two stages. In the first stage, a $s \times s$ window (named the search window) slides over the auxiliary image. The sliding direction is from top to bottom then from left to right. $s$ is a positive odd number. The horizontal and vertical step sizes (denoted by $q$) are the same and should be pre-specified. At each position, in the search window, elements of $\sigma$ whose $\iota$ with respect to the center pixel larger than $\varphi$ are categorized into the same group. To guarantee as many elements of $\sigma$ to be grouped as possible in the first stage, $1 \leq q \leq s$ is required.

After the first grouping stage, some elements of $\sigma$ may not be grouped. Therefore, in the second stage, we first locate the ungrouped element of the $\sigma$ which has the lowest row and column indexes in the EIT image, and group the elements of $\sigma$ in the $s \times s$ search window centered at the located element with the same $\varphi$ used in the first stage. Then, for the remaining ungrouped elements of $\sigma$, we continue locating the ungrouped element which has the lowest row and column indexes and perform the same grouping approach. We repeat this operation until all elements of $\sigma$ are grouped. In summary, the grouping process can be simply considered as sliding twice the $s \times s$ search window along the same direction over the auxiliary images to group all elements of $\sigma$.

During the grouping process, overlapping is allowed, leading to the grouping result:

$$\{\sigma_{g1}, \sigma_{g2}, \ldots, \sigma_{gG}\},$$

where $G$ is the number of groups, $1 \leq G \leq N$; $\sigma_{g\zeta} \cap \sigma_{g\tau} \neq \emptyset$ or $\sigma_{g\zeta} \cap \sigma_{g\tau} = \emptyset$ if $\zeta \neq \tau$, and $\bigcup_{\epsilon=1}^{G} \sigma_{g\epsilon} = \sigma$. $\zeta$, $\varsigma$ and $\epsilon$ are group indicators. The grouping method is simple and regular, and the result is controllable by tuning $s$ and $q$ once $f_n$ and $\iota$ are determined. An example of the grouping process is illustrated in Fig. 5.1 (b) ~ (d). Finally, the overlapping group lasso regularization term can be expressed by the following $l_{2,1}$ norm:

$$l_{2,1} = \sum_{\epsilon=1}^{G} \psi_\epsilon ||\sigma_{g\epsilon}||,$$

where, $\psi_\epsilon > 0$ represents the weight for the $\epsilon$th group.
5.3. Image Reconstruction based on OGLL

Figure 5.2: Principle of constructing the Laplacian matrix: $L_{n,:}$ denotes the $n^{th}$ row of $L$. The pink square represents the kernel center, which is also located at the $n^{th}$ pixel of the EIT image. Dark blue squares denote the 8-neighbors of the $n^{th}$ pixel. In $L_{n,:}$, the value at the pink pixel is set to 8, and that at the dark blue pixel is set to -1. Other values at light blue pixels are filled by zeros.

Algorithm 2: Dual-modal EIT Image Reconstruction based on OGLL

Input: Auxiliary image, $J$, $V$, $s$, $q$, $\varphi$, $\alpha$, $\beta_1$, $\beta_2$, $\eta_1$, $\eta_2$, $t_{max}$, $\vartheta$

1: Initialization: $\sigma \leftarrow 0_N$, $z \leftarrow 0_E$, $\lambda_1 \leftarrow 0_E$, $\lambda_2 \leftarrow 0_M$.
2: Conductivity grouping to construct (10) according to A, Section III.
3: while stopping criteria unsatisfied do
4: Solve problem (5.10) by (5.11);
5: Solve problem (5.12) by (5.14);
6: Update $\lambda_1$ by (5.16);
7: Update $\lambda_2$ by (5.17).
8: end while

Output: Calculated conductivity distribution.

5.3.2 The Laplacian Regularization

We will show later that group overlapping may lead to artefacts (see Fig. 5.7), i.e. the GOA, especially for relatively small $s$ and $q$. The GOA increases the rapid pixel intensity changes in the reconstructed EIT image. Inspired by (Y. Yang et al., 2014), the Laplacian regularization term is included to alleviate the negative influence of GOA. The continuous Laplacian of an image $\mathcal{I}(x,y)$ is defined as:

$$\mathcal{L}(x,y) = \frac{\partial^2 \mathcal{I}(x,y)}{\partial x^2} + \frac{\partial^2 \mathcal{I}(x,y)}{\partial y^2},$$  (5.6)
where \( x \in \mathbb{R} \) and \( y \in \mathbb{R} \) are coordinates of the image. As the Laplacian is sensitive to rapid image intensity changes, we might penalize the Laplacian of the EIT image to reduce GOA. For digital images, a small discrete convolutional kernel is usually adopted to approximate (5.6) and the discrete Laplacian can be calculated by the convolution. In this work, a \( 3 \times 3 \) kernel is chosen and the vectorized discrete Laplacian of the EIT image can be formulated as \( L \sigma \), where \( L \in \mathbb{R}^{N \times N} \) is the Laplacian matrix. The detailed description of the kernel and the Laplacian matrix construction is illustrated in Fig. 5.2.

### 5.3.3 The Proposed OGLL-based Algorithm

OGLL can be formulated as the following optimization problem:

\[
\min_{\sigma} \sum_{\varepsilon=1}^{G} \psi_{\varepsilon} \| \sigma_{\varepsilon} \| + \frac{\theta}{2} \| L \sigma \|^{2}
\]

s.t. \( J \sigma = V \),

(5.7)

where \( \theta > 0 \) denotes the parameter for the Laplacian regularization. (5.7) can be effectively solved by ADMM. By introducing an auxiliary variable \( z \in \mathbb{R}^{\Xi} \), (5.7) is reformulated as:

\[
\min_{\sigma, z} \sum_{\varepsilon=1}^{G} \psi_{\varepsilon} \| z_{\varepsilon} \| + \frac{\theta}{2} \| L \sigma \|^{2}
\]

s.t. \( z = F \sigma, J \sigma = V \),

(5.8)

where \( F \in \mathbb{R}^{\Xi \times N}, N \leq \Xi \leq N^{2} \), is a \((0, 1)\) matrix and each row has a unique 1. If \( n^{th} \) element of \( \sigma \) belongs to \( G \) groups, \( 1 \leq G \leq G \), there are \( G \) rows of \( F \) in each of which the \( n^{th} \) element is 1. Thus, the transformation of \( F \) duplicates the \( n^{th} \) element of \( \sigma \) \( G \) times and integrates them into \( z \). In other words, although elements of \( \sigma \) are overlapped, elements of \( z \) are completely non-overlapped. Furthermore, \( F^{T} F \) is a diagonal matrix, whose \( n^{th} \) diagonal element represents the number of groups the \( n^{th} \) element of \( \sigma \) belongs to. Especially in the case of non-overlapping grouping, \( F \) becomes a \( N \times N \) identity matrix. To solve (5.8), the augmented Lagrangian equation is firstly constructed:

\[
\min_{\sigma, z, \lambda_{1}, \lambda_{2}} \sum_{\varepsilon=1}^{G} \psi_{\varepsilon} \| z_{\varepsilon} \| + \frac{\theta}{2} \| L \sigma \|^{2} - \lambda_{1}^{T} (z - F \sigma) + \frac{\beta_{1}}{2} \| z - F \sigma \|^{2} - \lambda_{2}^{T} (J \sigma - V) + \frac{\beta_{2}}{2} \| J \sigma - V \|^{2},
\]

(5.9)
where $\lambda_1 \in \mathbb{R}^\Xi$, and $\lambda_2 \in \mathbb{R}^M$ are Lagrange multipliers and $\beta_1 > 0$ and $\beta_2 > 0$ are penalty parameters. Then, (5.9) can be split into the $\sigma$-subproblem and the $z$-subproblem, which are solved separately. From (5.9), the $\sigma$-subproblem can be expressed as:

$$
\sigma' = \arg\min_{\sigma} \frac{\theta}{2} \|L\sigma\|^2 + (\lambda_{1}^{(t-1)})^T F\sigma + \frac{\beta_1}{2} \|z^{(t-1)} - F\sigma\|^2
$$

$$
- \lambda_{1}^T J\sigma + \frac{\beta_2}{2} \|J\sigma - V\|^2,
$$

(5.10)

where superscript $t = 1, 2, 3, \ldots$ represents the iteration number. In this work, (5.10) is solved by one-step gradient descent, and its iteration equation is expressed as:

$$
\sigma' = \sigma^{(t-1)} - \alpha \left[ (\theta L^T L + \beta_1 F^T F + \beta_2 J^T J) \sigma^{(t-1)} - \left( \beta_1 F^T z^{(t-1)} - F^T \lambda_{1}^{(t-1)} - \beta_2 J^T V + J^T J \right) \sigma^{(t-1)} \right],
$$

(5.11)

where $\alpha$ is the iteration step length.

The $z$-subproblem can also be deduced from (5.9) and it is formulated as:

$$
z' = \arg\min_z \sum_{\varepsilon=1}^{G} \psi_{\varepsilon} \|z_{\varepsilon}^{(t)}\| - (\lambda_{1}^{(t-1)})^T z + \frac{\beta_1}{2} \|z - F\sigma'\|^2.
$$

(5.12)

Equation (5.12) is equivalent to solving the below problem:

$$
z' = \arg\min_z \sum_{\varepsilon=1}^{G} \left[ \psi_{\varepsilon} \|z_{\varepsilon}^{(t)}\| + \frac{\beta_1}{2} \left\| z_{\varepsilon}^{(t)} - (F\sigma')_{\varepsilon} - \frac{1}{\beta_1} (\lambda_{1}^{(t-1)})_{\varepsilon} \right\|^2 \right],
$$

(5.13)

which can be solved using group-wise soft thresholding:

$$
(z')_{\varepsilon} = \max \left( 0, ||\ell_{\varepsilon}|| - \frac{\psi_{\varepsilon}}{\beta_1} \right) \frac{\ell_{\varepsilon}}{||\ell_{\varepsilon}||}, \varepsilon = 1, 2, \ldots, G,
$$

(5.14)

where $\ell_{\varepsilon}$ is given by:

$$
\ell_{\varepsilon} = (F\sigma')_{\varepsilon} + \frac{1}{\beta_1} (\lambda_{1}^{(t-1)})_{\varepsilon}, \varepsilon = 1, 2, \ldots, G.
$$

(5.15)

Afterwards, the Lagrange multipliers are updated:

$$
\lambda_{1}^{(t)} = \lambda_{1}^{(t-1)} - \eta_1 \beta_1 (z' - F\sigma'),
$$

(5.16)

$$
\lambda_{2}^{(t)} = \lambda_{2}^{(t-1)} - \eta_2 \beta_2 (J\sigma' - V),
$$

(5.17)
where $\eta_1 > 0$ and $\eta_2 > 0$ are iteration step lengths. The stopping criteria are defined by two conditions. The first one is the maximum iteration $t_{\text{max}} \in \mathbb{Z}^+$ and the second one is the tolerance $\vartheta > 0$ which is defined as:

$$
\frac{|\sigma^{t+1} - \sigma^t|}{||\sigma^t||} < \vartheta.
$$

If any of the conditions are satisfied, OGLL will stop. We initialize $\sigma, z, \lambda_1$ and $\lambda_2$ with zero vectors. The implementation of OGLL is summarised in Algorithm 2.

**Remarks:** $\mathbf{0}$ represents the column 0-vector and the subscript accounts for its size. In this paper, the weights $\psi_i$ are always set as 1.

### 5.4 Simulation Study

In this section, we conduct numerical simulations to analyze the performance of the OGLL method. First, based on blocky phantoms, we compare OGLL with standard Tikhonov regularization (Golub, Hansen, & O’Leary, 1999), Structure-Aware Sparse Bayesian Learning (SA-SBL) (S. Liu et al., 2018), Kernel Method (Z. Liu & Yang, 2021b), and the dual-modal algorithm in (Gong et al., 2016) (named KMGS in this paper), and discuss the properties of the OGLL. Moreover, the performance of the given algorithms are compared based on thorax imaging. For a fair comparison, ADMM optimization for KMGS is implemented the same as in OGLL while the grouping method remains identical to that in the original paper. In this section, Relative Image Error and MSSIM are selected as the quantitative metrics. The definition of them is demonstrated in (3.27) and (3.28), respectively. The Relative Image Error is abbreviated as $\text{Err}$ in this chapter.
5.4. Simulation Study

Figure 5.3: Image reconstruction results based on blocky phantoms. Images from top to bottom correspond to case 1, case 2 and case 3, respectively. For case 1, the number of groups is 47 for OGLL-NGOA and 76 for OGLL-GOA; for case 2, the number of groups is 47 for OGLL-NGOA and 360 for OGLL-GOA; and for case 3, the number of groups is 201 for OGLL-NGOA and is 3228 for OGLL-GOA.

Figure 5.4: Images in the first row are simulated auxiliary images and those in the second row are results of modified K-Means in KMGS. The number of clusters is 20, 30, and 25 for case 1, case 2 and case 3 respectively. Numbers in the second row of images differentiate different groups rendering similar colors.
5.4. Simulation Study

5.4.1 Blocky Phantom Imaging

**Modelling**

We modelled the 16-electrode EIT sensor and added various inclusions as imaging targets. The resulting three types of conductivity distributions are labelled as case 1, case 2 and case 3. The simulated true conductivity images are illustrated in the first column of Fig. 5.3 and they correspond to case 1 ∼ 3 sequentially from top to bottom. For all cases, the background conductivity is set to 2 S/m. There are two rectangular inclusions for case 1. The conductivity of the left rectangle is set to 3.2 S/m and that of the right rectangle is set to 1.4 S/m. Case 2 simulates a huge circular inclusion whose conductivity is set to 0.5 S/m. For case 3, the conductivity of the uppermost smallest circular inclusion is set to 1.4 S/m. Starting from the rightest inclusion, the conductivity of the rest four inclusions is clockwise set to 1.4 S/m, 0.4 S/m, 0.9 S/m and 0.9 S/m. The auxiliary images are also simulated by assigning digit 1 to pixels of the inclusions and the background pixels are set to 0.5. The generated auxiliary images are illustrated in the first row of Fig. 5.4.

**Parameter Settings**

Parameters for each algorithm are selected based on trials to obtain the results as best as possible. The regularization parameters of Tikhonov regularization are set as 0.00001, 0.0001, and 0.0003 for case 1, case 2, and case 3, respectively. For SA-SBL, the maximum iteration number, tolerance, and cluster size are set as 5, 10^{-5}, and 4 for all cases. The pattern coupling factors are set as 0.3, 2, and 0.8 for cases 1, 2, and 3 sequentially. For the Kernel Method, all parameters are the same for the three cases. The feature window size and the search window size are set as 3 and 21, respectively. The number of nearest neighbors $k$NN is set as 441, and the variance of the Gaussian kernel is fixed as 20. In addition, the maximum iteration number is set as 500, and the iteration step for the gradient is selected as 10. For all cases, KMGS takes the same weighting parameter (0.01) for modified K-Means clustering, and the number of clusters is set to 20, 30, and 25 for cases 1, 2, and 3.

In later discussions, we group conductivities based on two types of search windows. One type of search windows usually causes the G OA phenomenon if we set $\theta$ to 0. The results based on this type of search windows are labeled as OGLL-GOA. The other type of search windows will not result in the G OA phenomenon if we set $\theta$ to 0, and the results are labeled as OGLL-NGOA. Usually, the search window size of OGLL-NGOA is larger than that of OGLL-GOA. When we mention OGLL, we refer to both OGLL-GOA and OGLL-NGOA. For a specific case, parameters for OGLL-GOA and OGLL-NGOA are usually different. Detail settings of OGLL-GOA and OGLL-NGOA and parameters of KMGS (except the number of clusters and the weighting parameter) are illustrated in Table 5.1.
Figure 5.5: Examples of grouping results of OGLL. The first row is part of the results based on the parameters of case 1 of OGLL-NGOA in Table 5.1 and there are 47 groups in total. The second row is part of the results based on the parameters of case 2 of OGLL-GOA in Table 5.1 and there are 360 groups in total. For each image, pixels in the white region belong to the same group. Pink curves represent the boundaries of inclusions.

Figure 5.6: 1D profile comparison for case 1. (a) shows 1D profiles on the horizontal line across the center of the imaging region. Both (b) and (c) display the 1D profiles on the vertical line across the imaging region center. All images share the same legend. The curve of OGLL-NGOA is invisible in (b) because it is hidden by other curves.
5.4. Simulation Study

Figure 5.7: GOA phenomenon in OGLL-GOA for case 1 and case 2 at selected iteration steps (1, 10, 100, 1000). For numbers under each image, the top one is Err and the bottom one is MSSIM.

Results and Discussion

Fig. 5.3 compares OGLL with selected algorithms in the three cases. The voltage data is noise-free. The clustering results of the KMGS are shown in the second row of Fig. 5.4. Part of the grouping results of OGLL is illustrated in Fig. 5.5. The results show the performance of single-modal-based algorithms is generally inferior to the multi-modal-based algorithms. This situation is indicated by visualization and quantitative metrics, i.e. the Err and MSSIM. The reason is that multi-modal methods utilize complementary information from other imaging modalities, mitigating the ill-posedness of the EIT inversion. Fig. 5.6 compares 1D profiles of case 1 of different algorithms. The results further visually demonstrate that dual-modal methods are generally superior to single-modal methods. Among dual-modal methods, OGLL-NGOA achieves the best performance. OGLL-GOA also show a better BA suppression and competitive structure preservation ability compared to other algorithms. The quality of the reconstructed inclusions based on OGLL-GOA is similar to those based on Kernel Method and KMGS, while OGLL-GOA performs better than Kernel Method and is akin to KMGS on BA suppression. Nevertheless, quantitative metrics indicate the performance of both OGLL-GOA and OGLL-NGOA is generally superior to other given algorithms.

We demonstrate the effect of Laplacian regularization based on cases 1 and 2. Usually, the EIT image can be reconstructed well based on OGLL-NGOA. The reconstructed images of cases 1 and 2 based on OGLL-NGOA are shown in the seventh column of the Fig. 5.3. However, when we set $\theta = 0$ and keep other parameters for OGLL-GOA, GOA appears (see Fig. 5.7). The GOA originated from the search window size can hardly be eradicated by tuning
other parameters and the results also show that such a phenomenon remains when iteration increases. Reconstructed images of OGLL-GOA with activated Laplacian regularization are displayed in the sixth column of the Fig. 5.3. These results indicate that Laplacian regularization mitigates the issue of GOA while the image quality degrades. The degradation of image quality is reasonable because the Laplacian regularization not only ‘punishes’ the GOA but also blurs the edges of the inclusions. Nevertheless, it is conspicuous that OGLL provides flexible and controllable grouping and reconstruction strategies, and the Laplace regularization guarantees an accepted reconstruction when encountering the GOA.

Based on case 3, Fig. 5.8 compares the voltage noise resistance ability of algorithms. We set a series of different SNRs for voltage data and display the Err and the MSSIM of given algorithms. The results demonstrate that OGLL can resist the widest range of SNRs meanwhile maintaining the best metric values, which indicates the proposed OGLL has the best performance on voltage noise resistance.

The convergence analysis of OGLL is illustrated in Fig. 5.9. We observe that Err decreases with iterations and MSSIM increases with iterations, indicating the correct convergence property of the OGLL. However, oscillations exist due to two reasons. First, ADMM-based algorithms are not guaranteed monotonically decreasing (G. Wang & Qi, 2014a). Second, we use one-step gradient descent with fixed step length to solve the $\sigma$-subproblem, which increases the possibility of oscillation. Convergence curves vary with different cases since they are related to true conductivity distributions.

**Figure 5.8:** Voltage noise resistance ability comparison: Err and MSSIM change with different SNRs. The plots share the same legends.
5.4. Simulation Study

Figure 5.9: Convergence curves: Err and MSSIM change with iterations.

Figure 5.10: Err and MSSIM variation with \( s \) and \( q \) change for OGLL-NGOA and OGLL-GOA.
5.4 Simulation Study

Figure 5.11: The left image is the simulated CT image of the thoracic cross section and the right image is the simulated true thoracic EIT image.

Table 5.2: Parameter settings of OGLL and KMGS for thoracic imaging.

<table>
<thead>
<tr>
<th></th>
<th>s</th>
<th>q</th>
<th>θ</th>
<th>α</th>
<th>β₁</th>
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<td>\</td>
<td>\</td>
<td>0</td>
<td>0.024</td>
<td>0.12</td>
<td>0.12</td>
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<td>OGLL-NGOA</td>
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<td>0</td>
<td>0.009</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>OGLL-GOA</td>
<td>31</td>
<td>5</td>
<td>0.15</td>
<td>0.007</td>
<td>0.25</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Fig. 5.10 takes case 1 as an example to analyse the influence of q and s on OGLL-NGOA and OGLL-GOA. Suppose suitable \( f_n \), \( t \) and \( ϕ \) are defined, among OGLL parameters, s and q determine the grouping result, and further influence the reconstruction quality. Fig. 5.10 displays the Err and MSSIM variation with q or s meanwhile freezing other parameters. The results show there is a relatively wide range to select q or s while retaining a satisfactory result, indicating reduced complexity of parameter tuning.

There are several parameters to be tuned in OGLL. Therefore, it is worth introducing the parameter tuning experience. In this work, we adopt fixed \( η_1, η_2, t_{\text{max}}, θ \) and \( ϕ \), and always set the same values for \( β_1 \) and \( β_2 \). Only s, q, θ, α, and \( β_1 \) (or \( β_2 \)) require tuning. The initial value of s is set according to the inclusion’s size in the auxiliary image and q is set to \((s - 1)/2\) to make groups partially overlap. In this study, the algorithm works correctly when we set the initial \( β_1 \) and \( β_2 \) both to 5. For both OGLL-NGOA and OGLL-GOA, the initial θ is set to 0. The next step is to select a reasonable starting point of α. One can begin from a large value, e.g. 100, and gradually decrease α by a factor of 0.1 until the quality of the reconstructed image improves with the increase of iterations. 0.01 is always selected as the initial α in this study. Afterwards, each parameter should be carefully tuned by the method of control variables.
5.4. Simulation Study

![Figure 5.12: Comparison of thoracic EIT image reconstruction. (a) ~ (f) sequentially correspond to results of Tikhonov regularization, SA-SBL, Kernel Method, KMGS, OGLL-GOA and OGLL-NGOA. For (d) the left image is the reconstruction and the right is the result of K-Means clustering. There are 15 clusters. For (e), the left image is the reconstruction with Laplacian regularization and the right one is the reconstructed image without Laplacian regularization. For numbers under the result of each algorithm, the upper one is Err and the lower one is MSSIM. There are 138 groups for both OGLL-NGOA and OGLL-GOA.](image)

5.4.2 Thoracic Imaging

Modelling

We modelled a cross-section of the human thorax to evaluate the performance of OGLL (see Fig. 5.11). Refer to (Z. Li et al., 2019), the surface contact impedance between electrodes and human skin is $10^{-4} \, \Omega \cdot m^{-1}$, and the left image of the Fig. 5.11 is the modeled CT image with 100 doses. Refer to (K. Zhang et al., 2020), the background conductivity, and the conductivity of the lungs and the heart are set to 0.24 S/m, 0.1 S/m and 0.5 S/m, respectively. The ground truth image is the right image of Fig. 5.11.

Parameter Settings

Parameter settings are based on trial and error. For Tikhonov regularization, the regularization parameter is set to 0.0005. For SA-SBL, the maximum iteration number, tolerance, cluster size, and the pattern coupling factor are set as 5, $10^{-5}$, 4 and 0.16, respectively. For the Kernel Method, the search window size and variance of the Gaussian kernel are set as 37 and 10, respectively. Other parameters are the same as those in the blocky phantom study. The weighting parameter for modified K-Means clustering in KMGS is 0.001 and the number of clusters is 15. Other parameters of KMGS and parameters of OGLL-NGOA and OGLL-GOA are given in Table 5.2. Parameters not shown in Table 5.2 are the same as those in Table 5.1.
5.4. Simulation Study

Table 5.3: Parameter settings of OGLL and KMGS for experimental phantom imaging.

<table>
<thead>
<tr>
<th></th>
<th>s</th>
<th>q</th>
<th>θ</th>
<th>α</th>
<th>β₁</th>
<th>β₂</th>
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<tbody>
<tr>
<td>KMGS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>\</td>
<td>\</td>
<td>0</td>
<td>0.035</td>
<td>0.08</td>
<td>0.08</td>
</tr>
<tr>
<td>Case 2</td>
<td>\</td>
<td>\</td>
<td>0</td>
<td>0.035</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>Case 3</td>
<td>\</td>
<td>\</td>
<td>0</td>
<td>0.04</td>
<td>0.045</td>
<td>0.045</td>
</tr>
<tr>
<td>OGLL-NGOA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>29</td>
<td>8</td>
<td>0</td>
<td>0.008</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Case 2</td>
<td>29</td>
<td>8</td>
<td>0</td>
<td>0.008</td>
<td>0.17</td>
<td>0.17</td>
</tr>
<tr>
<td>Case 3</td>
<td>29</td>
<td>8</td>
<td>0</td>
<td>0.008</td>
<td>0.08</td>
<td>0.08</td>
</tr>
<tr>
<td>OGLL-GOA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case 1</td>
<td>11</td>
<td>4</td>
<td>0.3</td>
<td>0.01</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>Case 2</td>
<td>15</td>
<td>4</td>
<td>0.1</td>
<td>0.008</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Case 3</td>
<td>17</td>
<td>5</td>
<td>0.04</td>
<td>0.008</td>
<td>0.25</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Results and Discussion

The reconstructed EIT images and quantitative metrics are shown in Fig. 5.12. The result of SA-SBL is poor. There are two main reasons. First, BA is severe for the irregular sensing region. Second, SA-SBL is more suitable for sparse conductivity distribution rather than non-sparse situations. The Kernel method reconstructs the most homogeneous lungs and heart among given algorithms while the non-sparse background is noticeable. These phenomena are also clearly indicated in Fig. 5.6. For Fig. 5.12 (e), GOA is alleviated by the Laplacian regularization, which is consistent with the blocky phantom study. Compared with other algorithms, OGLL-NGOA and OGLL-GOA present superior performance, evidenced by quantitative metrics. Especially, OGLL-NGOA and OGLL-GOA recover the most accurate conductivity contrast levels, by comparing the color distribution of the reconstructed image with the ground truth.

5.5 Real-world Experiments

5.5.1 Phantom Fabrication and Data Collection

In experiments, we used phosphate-buffered saline as the reference conductivity (1.898 S/m). A total of five objects were selected and added to the imaging region into three groups labelled as case 1, case 2 and case 3 from top to bottom in the first column of Fig. 5.13. The first object is a conductive hexagonal prism (red arrow in the figure), whose conductivity is higher than the saline. The other objects are either non-conductive regular prisms/cylinders or non-conductive irregular prisms/cylinders, whose conductivities are lower than saline. Non-conductive objects were fabricated using stereolithography (SLA) with black resin (FormLabs Inc., MA).
5.5. Real-world Experiments

EIT data were collected using the Edinburgh EIT system (Y. Yang & Jia, 2017b). The adjacent strategy was adopted (Brown & Seagar, 1987) and the frequency of the excitation current was 10 kHz. A digital camera placed over the EIT sensor was used to collect the auxiliary images. The direct outputs of the camera are RGB images. We first converted them into grey-scale images (we call them original auxiliary images). We down-sampled the original auxiliary images into the EIT image size to acquire the expected auxiliary images. The original auxiliary images are illustrated in the first row of Fig. 5.14.

5.5.2 Parameter Settings

Parameter selection for each algorithm is based on trial and error. For all experiments, the Tikhonov regularization parameter is set to 0.005. For SA-SBL, the maximum iteration number, tolerance, the cluster size, and the pattern coupling factor are set as $5, 10^{-5}, 4$ and 0.03 for all cases. Regarding the Kernel Method, variances of the Gaussian kernel are set to 18, 3 and 3 for case 1, case 2 and case 3 respectively. Other parameters are the same as those described in 2)-B, Section IV. The number of clusters for modified K-Means in KMGS is 30 for all cases and the values of the weighting parameter are 0.08, 0.08 and 0.065 for cases 1, 2, and 3, respectively. Parameters of OGLL and KMGS related to ADMM are given in Table 5.3. Parameters not shown in Table 5.3 are the same as those in Table 5.1.

5.5.3 Results and Discussion

Fig. 5.13 shows the EIT image reconstruction results. The clustering results of KMGS are given in the second row of Fig. 5.14. In Fig. 5.13, there are two columns for OGLL-GOA. The left column is the reconstructed images with the Laplacian regularization and the right column is the reconstructed images without the Laplacian regularization. Compared with dual-modal methods, single-modal algorithms have less ability for structure preservation. Similarly to the simulation, the kernel method can reconstruct phantoms with homogeneous conductivity distribution but has limitations in eliminating the BA. The KMGS performs better than the kernel method while it is inferior to OGLL-NGOA, which can be indicated by the homogeneity of the background and objects. For OGLL-GOA, when we set the $\theta$ to non-zero numbers, the GOA is reduced. These experimental results further prove the effectiveness of the Laplacian regularization to mitigate the GOA though losing part of structural information. Nevertheless, OGLL-GOA generates EIT images close to the ground truth.

It is noticeable the boundaries in the auxiliary images are distinct in simulation and real experiments in this study. Good structural image quality could usually be gained for common auxiliary imaging modalities, such as CT and optical imaging. Therefore, $f_n$ and $i$ adopted in this work can perform well in these situations. However, when the boundaries in the auxiliary images are not clear, $f_n$ and $i$ used in this work may lead to inaccurate grouping. Therefore, new definitions of $f_n$ and $i$ should be investigated.
5.6 Summary

This chapter proposed a segmentation-free dual-modal EIT image reconstruction algorithm named OGLL. OGLL integrates the structural information of the auxiliary image into EIT inversion through overlapping group lasso. Combining the overlapping group lasso with Laplacian regularization, the choice range of the grouping parameters is expanded. Simulation studies and real-world experiments demonstrate the superiority of the proposed OGLL in improving the EIT image quality in terms of structure preservation, background artifact suppression,
5.6. Summary

and conductivity contrast differentiation. Future work will extend this method to 3D image reconstruction and explore its application in 3D cell culture imaging. In addition, $f_i$ and $t$ definitions for various auxiliary imaging modalities will also be comprehensively investigated in the future.
6.1 Introduction

Based on the dual-modal imaging framework shown in Fig. 1.1, Chapters 3 to 5 developed three model-based algorithms: IGGS, Kernel Method, and OGLL. Although we aimed to enhance the performance and utility of these algorithms, they still have their limitations to varying degrees. The common drawback is that these iterative algorithms are time-consuming and require several parameters to be tuned, which limits their broader applications.

Deep learning (DL) has recently revolutionized Computer Vision (CV) and Natural Language Processing (NLP) and demonstrated great potential in tissue engineering. DL-based methods can overcome specific limitations of model-based algorithms, such as reducing inference time and eliminating the need for parameter tuning.

Targeting quantitative 3D cell culture imaging, this Chapter reports a learning-based impedance-optical dual-modal imaging framework that can be extended to other tissue engineering applications. The framework comprises three components, i.e., an impedance-optical dual-modal sensor, the guidance image processing algorithm, and a deep learning model named multi-scale feature cross fusion network (MSFCF-Net) for information fusion. The MSFCF-Net has two inputs, i.e., the EIT measurement and a binary mask image generated by the guidance image processing algorithm, whose input is an RGB microscopic image. The network then effectively fuses the information from the two different imaging modalities and generates the final conductivity image. We assess the performance of the proposed dual-modal framework by numerical simulation and MCF-7 cell imaging experiments. The results show that the proposed method could improve the image quality notably, indicating that impedance-optical joint imaging has the potential to reveal the structural and functional information of tissue-level targets simultaneously. The contributions of this chapter are summarized:
6.1 Introduction

Figure 6.1: Schematic of the impedance-optical dual-modal imaging framework.

- Compared with single-modal methods, the proposed framework can generate EIT images with more accurate shapes by introducing optical imaging, thereby leading to more precise conductivity distribution estimation.
- The framework develops a new indirect information fusion approach that addresses the challenge of directly using the optical image to train the deep learning model. This approach can be extended to other learning-based multi-modal image reconstruction scenarios with similar issues, e.g., where it is impossible to collect auxiliary images for training, or there are insufficient auxiliary images.

6.2 Impedance-Optical Dual-Modal Imaging Framework

This section proposes a learning-based impedance-optical dual-modal imaging framework (see Fig. 6.1) to improve EIT image quality for 3D cell imaging. It consists of three components, i.e., the impedance-optical miniature sensor, the guidance image processing algorithm, and a deep learning model. First, the impedance-optical sensor will simultaneously output a frame of voltage measurements and an RGB microscopic image named the guidance image ($I^G$). Then, the guidance image processing algorithm will convert $I^G$ into its corresponding mask image ($I^M$). Finally, $I^M$ and the voltage measurements are fed into a deep-learning model to generate the reconstructed EIT image.

6.2.1 Impedance-optical Dual-modal Sensor

The dual-modal sensor (see Fig. 6.2) combines a miniature 16-electrode EIT sensor with a digital microscope (Digital USB Microscope 1.3M, RS Components Ltd). The EIT sensor is manufactured on a Printed Circuit Board (PCB). A transparent glass substrate is attached at the bottom of the sensing area to support cells and enable optical imaging. The height and
6.2. Impedance-Optical Dual-Modal Imaging Framework

Figure 6.2: Impedance-optical dual-modal sensor. (a) EIT sensor structure. (b) The manufactured dual-modal sensor.

Figure 6.3: An illustration of the guidance image processing procedure. The dashed square represents the circumscribed square region of the circular sensing region. The numbers mean the number of pixels for each side of the square.

diameter of the sensing chamber are 1.6 mm and 14 mm, respectively. The 16 gilded micro-electrodes are manufactured using the half-hole process and distributed at the periphery of the sensing area. The digital microscope is placed over the sensing chamber and is calibrated well to make its view field the same as the sensing area. This dual-modal sensor can then simultaneously record the cells’ visual profiles and EIT measurements.

6.2.2 Guidance Image Processing

Guidance image processing containing four steps converts the guidance image $I^g$ into its corresponding mask image $I^m$ (see Fig. 6.3). The size of $I^m$ is the same as that of the expected EIT image, which occupies a circular region inscribed in a $64 \times 64$ square region, while the size of $I^g$ is much larger than it. $I^g$ also occupies a circular region, but this circle inscribes in a $406 \times 406$ square region. It should also be noted that $I^g$ has three color channels, i.e., R, G and B. Therefore, this algorithm starts with the processing of the high-resolution RGB image $I^g$.

In $I^g$, the illumination often causes shadow, which is invalid information and significantly affects the target segmentation. Besides, as the structure of the targets is only desired, preservation of color has seldom significance. Therefore, the first step is to obtain the 1D illuminant invariant image $I^{inv}$ of $I^g$ following the methods proposed by Finlayson et al. (Finlayson et al., 2009) in order to convert $I^g$ into a grey-scale image while removing the influence of illumination. The
equation is formulated as:

\[ I^{\text{inv}}(r, c) = \exp(\chi^{\text{inv}}_1(r, c) \cos(\Theta) + \chi^{\text{inv}}_2(r, c) \sin(\Theta)) \] (6.1)

where \( r \) and \( c \) are pixel indexes. \( \Theta \) is the projection direction in the 2D log-chromaticity space of \( I^{\text{inv}} \) which is a constant for a specific camera. This direction leads to the minimum Shannon's entropy for \( I^{\text{inv}} \) and can be approximately obtained by traversing every integer angle from 1° to 180°. \( \chi^{\text{inv}}_1(r, c) \) and \( \chi^{\text{inv}}_2(r, c) \) is expressed as:

\[ [\chi^{\text{inv}}_1(r, c), \chi^{\text{inv}}_2(r, c)]^T = U \rho(r, c). \] (6.2)

Here, \( U \) is a \( 2 \times 3 \) orthogonal matrix and take the value of \( U = [v_1, v_2]^T, v_1 = [\frac{1}{\sqrt{2}}, -\frac{1}{\sqrt{2}}, 0]^T, v_2 = [\frac{1}{\sqrt{6}}, \frac{1}{\sqrt{6}}, -\frac{2}{\sqrt{6}}]^T. \) \( \rho(r, c) \) is defined by:

\[ \rho(r, c) = \left[ \ln \left( \frac{R(r, c)}{\Sigma(r, c)} \right), \ln \left( \frac{G(r, c)}{\Sigma(r, c)} \right), \ln \left( \frac{B(r, c)}{\Sigma(r, c)} \right) \right]^T \] (6.3)

where \( \Sigma(r, c) = \sqrt{R(r, c)G(r, c)B(r, c)} \) and \( R(r, c), G(r, c), \) and \( B(r, c) \) are the three components of a color image.

Then, the binary version of \( I^{\text{inv}} \) can be generated by using the following thresholding segmentation method:

\[ I^{\text{bw}}(r, c) = \begin{cases} 0, & \text{if } I^{\text{inv}}(r, c) < \beta \\ 1, & \text{if } I^{\text{inv}}(r, c) \geq \beta \end{cases} \] (6.4)

where \( I^{\text{bw}} \) denotes the binary image after thresholding. The threshold value \( \beta \) is selected based on empirical trials. However, such a method may lead to irregular boundaries and randomly distributed white pixels. To address this issue, the third step applies morphological operations to \( I^{\text{bw}} \) to acquire a clean binary image with boundary-regular targets. In this paper, open operation (6.5) and dilation operation (6.6) are successively applied to reduce background irrelevant information and recover accurate target profiles. The two operations are defined as (Gonzales & Wintz, 1987):

\[ I^{\text{bw}}_1 = I^{\text{bw}} \circ S = \bigcup \{ (S)_z | (S)_z \subseteq I^{\text{bw}} \} \] (6.5)

\[ I^{\text{bw}}_2 = I^{\text{bw}}_1 \oplus S = \{ z | (S)_{\hat{z}} \cap I^{\text{bw}}_1 \neq \emptyset \} \] (6.6)

where, \( I^{\text{bw}} \circ S \) means \( I^{\text{bw}} \) is opened by the structuring element \( S \) and \( I^{\text{bw}}_1 \oplus S \) means \( I^{\text{bw}}_1 \) is dilated by \( S. \) \((S)_z \) and \( \hat{S} \) are defined as (Gonzales & Wintz, 1987):

\[ (S)_z = \{ k | k = a + z, a \in S \} \] (6.7)
6.2. Impedance-Optical Dual-Modal Imaging Framework

Figure 6.4: Architecture of MSFCF-Net. Note, the color of arrow is only for indicating the feature maps flowing to different function block. BN-V and BN-M are the layers in dashed gray squares.

\[
\hat{S} = \{ w | w = -a, a \in S \} 
\]

(6.8)

where \( z = (z_1, z_2) \) is a fixed point in the image space where \( I^{bw} \) and \( I^{bw1} \) exist.

\( I^{bw2} \) already provides the expected structural information, but it cannot be directly used as the input of the MSFCF-Net. As stated at the beginning of this subsection, the size of \( I^m \) is required to be the same as that of the EIT image. In addition, the height and width of images generated by the first three steps (i.e., \( I^{inv}, I^{bw} \) and \( I^{bw2} \)) is the same as those of \( I^r \). Therefore, the final step is to down-sample \( I^{bw2} \) into a smaller circular image internally tangent with a 64 \( \times \) 64 square region. The resulting smaller image is the \( I^m \), and it is exactly the tiny version of \( I^{bw2} \).

6.2.3 Multi-scale Feature Cross Fusion Network

MSFCF-Net reconstructs an EIT image \( I^{eit} \) from a frame of voltage measurements \( \Delta V^* \in \mathbb{R}^{104} \) and a mask image \( I^m \). We describe \( I^{eit} \) and \( I^m \) with a tensor of size \( C \times 64 \times 64 \), where \( C = 1 \) denotes the number of channels for a multi-channel image. \( \Delta V^* \) and \( I^{eit} \) are defined by:

\[
\Delta V^* = \frac{V_{\sigma_1} - V_{\sigma_0}}{V_{\sigma_0}},
\]

(6.9)

\[
I^{eit} = -\frac{\sigma_1 - \sigma_0}{\sigma_0}.
\]

(6.10)
6.2. Impedance-Optical Dual-Modal Imaging Framework

Although td-EIT aims to recover \( \Delta \sigma = \sigma_1 - \sigma_0 \) from \( \Delta V = V_{\sigma_1} - V_{\sigma_0} \), in this work, we adopt the relative changes format to facilitate the training of the deep learning model (Ioffe & Szegedy, 2015).

Our goal is to learn an end-to-end mapping \( F \) from \( \Delta V^* \) and \( I^m \) to \( I^{\text{eit}} \). Given a training dataset \( \{ \Delta V^*_i, I^m_i, I^{\text{eit}}_i \}_{i=1}^N \), the problem can be described as:

\[
\hat{\theta} = \arg\min_{\theta} \frac{1}{N} \sum_{i=1}^{N} L(F_{\theta}(\Delta V^*_i, I^m_i), I^{\text{eit}}_i) + \frac{\lambda}{2} ||\theta||^2_2
\]  

(6.11)

where the second term is \( l_2 \) regularization with a penalty parameter \( \lambda \), which can reduce over-fitting. \( \theta = \{ W, b \} \) represents the weights and bias of MSFCF-Net. \( L \) is the loss function to minimize the difference between \( I^{\text{eit}}_i \) and \( F_{\theta}(\Delta V^*_i, I^m_i) \). As EIT image reconstruction is a regression problem, the mean squared error loss function is used, and \( L \) is defined as:

\[
L(F_{\theta}(\Delta V^*_i, I^m_i), I^{\text{eit}}_i) = ||F_{\theta}(\Delta V^*_i, I^m_i) - I^{\text{eit}}_i||^2_2
\]  

(6.12)

The architecture of MSFCF-Net is shown in Fig. 6.4. Subnetworks in MSFCF-Net can be divided into three categories, i.e. the backbone networks, dual-modal feature fusion modules, and multi-scale feature fusion modules.

**Backbone Networks (BN)**

The backbone network extracts latent features from inputs. Thus, this network should have a good ability for feature extraction. The Darknet as the backbone of YOLOV3 has proved effective and powerful in feature extraction (Redmon & Farhadi, 2018). Inspired by its architecture, we designed the Darknet-like backbone networks for our application. The backbone network for voltage measurements (BN-V) has three additional fully connected layers followed by a reshape operation because of the dimension difference between \( \Delta V^* \) and \( I^m \) (see Fig. 6.4). The output of the reshape operation is a feature map with the size of \( 1 \times 64 \times 64 \). The rest of BN-V is the same as the backbone network for mask image (BN-M), which consists of five residual blocks denoted by Res(n). Res(n) starts with left-and-upper zero padding followed by a \texttt{Conv + Leaky ReLU} unit with \texttt{Kernel Size} = \( 3 \times 3 \), \texttt{Stride Step} = \( 2 \), and the number of kernels is twice as that of input feature maps. Then \( n \) residual units (represented by Res Unit, see Fig. 6.4) follow. The idea of Res Unit is proposed in (He, Zhang, Ren, & Sun, 2016), in which the short connection can make the deep network easier to train. Therefore, the combination of the mentioned components in Res(n) will make the height and width of the output feature maps half of those of input feature maps while the number of feature maps doubles.
6.2. Impedance-Optical Dual-Modal Imaging Framework

Figure 6.5: Architecture of DMFF. The purple block means the mapping $f_A$, $f_A$ equals to $f^{CA}$ for DMFFM-V1 and $f_A$ equals to $f^{SA} \circ f^{CA}$ for DMFFM-V2. The meaning of other components is the same as those of legends in Fig. 6.4.

Dual-modal Feature Fusion Module (DMFF)

Dual-modal Feature Fusion Modules (DMFF) fuse information from different sources (see Fig. 6.5). To maintain the main information and eliminate the trivial ones, the attention mechanism originally used in natural language processing (Bahdanau, Cho, & Bengio, 2014) is adopted in DMFF. As the feature maps generated by each layer in CNN have both channel dimension and spatial dimension, there are two types of attention mechanism, i.e., channel-wise attention and spatial-wise attention. In BN-V and BN-M, the spatial dimension gradually decreases with the increase of the number of layers. For feature maps with a small spatial dimension, the spatial information is lost, and information carried by this type of feature maps is usually called semantic information. The spatial relationship between each element of the feature maps is trivial. Therefore, there are two types of DMFF in MSFCF-Net, i.e., DMFF-V1 and DMFF-V2 (see Fig. 6.4). DMFF-V1 corresponds to the feature maps with large spatial dimension, and it will incorporate both channel-wise attention and spatial-wise attention. DMFF-V2 corresponds to the feature maps with small spatial dimensions, and it will only incorporate channel-wise attention. The implementation of attention mechanisms adopts the convolutional block attention modules proposed in (Woo, Park, Lee, & Kweon, 2018), which is proved to be an effective and efficient method. Suppose the mapping of the channel attention module in CBAM is denoted by $f^{CA}$ and that of the spatial attention module is denoted by $f^{SA}$, the mappings of both DMFF-V1 and DMFF-V2 can be uniformly expressed as:

\[
\begin{align*}
S_v &= f_A \left( f^{CL}_{1,1} \left( f^{CL}_{3,1} \left( f^{CL}_{1,1} (M) \right) \right) \right), \\
S_m &= f_A \left( f^{CL}_{1,1} \left( f^{CL}_{3,1} \left( f^{CL}_{1,1} (M) \right) \right) \right), \\
M_{dm} &= R^3 (S_v, S_m),
\end{align*}
\]

(6.13) (6.14) (6.15)
where $M_v$ is the feature map from BN-V and $M_m$ is the feature map from BN-M. The size of the feature maps $S_v$, $S_m$, $M_{dm}$, $M_v$, and $M_m$ is the same. $f^A$ equals to $f^{CA}$ for DMFFM-V1 and equals to $f^{SA} \circ f^{CA}$ for DMFFM-V2, which is the only difference between the two modules. $f^{CL}$ denotes the mapping for Conv + Leaky ReLU unit. The first subscript means the kernel size and the second means the convolution step used in the convolution layer in this unit. $[\cdot, \cdot]$ denotes the concatenation operation and $R^3$ means the mapping of Res(3).

Multi-scale Feature Fusion Module (MSFF)

Feature maps of different scales will provide information on different scales. It will generate a more precise result if the information of different scales can be integrated together. Many work in computer vision and image processing demonstrates that fusing feature maps of different scales is an efficient way to improve the performance of the network (W. Liu et al., 2016; Redmon & Farhadi, 2018; Ronneberger, Fischer, & Brox, 2015). In addition, Chen et al. (Chen et al., 2020) and Li et al. (F. Li et al., 2020) both adopted this method in their work on EIT image reconstruction and showed good results. MSFCF-Net also adopts the same idea and the multi-scale feature fusion module (MSFF, see Fig. 6.6) undertakes this function. MSFF module uses a simple way to perform information fusion. First, the spatial dimension of low-scale feature maps will be enlarged twice by transposed convolutional layers followed by the Leaky ReLU layer. Then, the output of the Leaky ReLU layer and the output of the network block before the current block will be added together in MSFF. The addition operation here is inspired by the work on human eye-fixation prediction, where the authors also face a dual-modal information fusion problem and fuse information of different scales by addition operation (W. Liu, Zhou, & Luo, 2020). Like YOLOV3, the initial fused feature maps will be fed into multiple layers for thorough information fusion. Instead of using successive convolutional layers, the basic module in BN, i.e. Res(n), is used in MSFF to conduct post-information fusion. Because this module has a satisfactory feature extraction ability while it can prevent
the degradation of the network (He et al., 2016). Finally, the output of the current MSFF will be the input of the next MSFF. The mapping of MSFF can be represented as:

\[
M_{ms} = R^3 \left( M_h + f_{TCL}^{2,2} (M_l) \right),
\]

where \(M_l\) is the low-scale feature map and \(M_h\) is the high-scale feature map. The size of the output feature map \(M_{ms}\) is the same as that of \(M_h\). \(f_{TCL}^{2,2}\) represents the mapping for Transposed Conv + Leaky ReLU unit. The first subscript means the kernel size and the second represents the convolutional step in the convolution layer of this unit. \(R^3\) means the mapping of Res(3).

### 6.3 Data Generation and Experimental Setup

#### 6.3.1 Sensor Modelling and Dataset Generation

We establish the training, validation and test sets to train and evaluate the proposed MSFCF-Net. In COMSOL Multiphysics we modelled the 2D 16-electrode circular EIT sensor and solved the forward problem of EIT to generate simulation data. The EIT forward problem is approximately solved by the Finite Element Method (FEM), which is the primary source leading to the modelling error. We adopted the time-difference imaging method, which could eliminate the common errors to a certain extent.

To make the deep learning model suitable for 3D cell culture imaging, specifically for 3D cell spheroids imaging, we consider multi-level, multi-circular-object conductivity distributions. In the sensing region, we generate four types of data and a sample belonging to a certain type of data includes a fixed number of objects (from one to four). For a certain type of data, for example, the one including three objects, we assign three non-overlapping circular objects with random diameters (from 0.07 \(d\) to 0.3 \(d\), \(d\) is the diameter of the sensing area), positions, and conductivity values (from 0.0001 \(S \cdot m^{-1}\) to 0.0475 \(S \cdot m^{-1}\)). The background conductivity is 0.05 \(S \cdot m^{-1}\). As the spatial resolution of EIT is about 10% of the sensor diameter (Metherall et al., 1996), we cannot set the diameter of the object too small. The maximum diameter of the objects can cover most 3D cell culturing situations. Thus, the setting of the object diameter range is reasonable. For conductivity settings, if the conductivity of a certain object is very close to the background conductivity, the voltage measurements can hardly be distinguished from those without such object in the sensing region. Therefore, the criteria avoid that the conductivity of an object is too close to the background conductivity.
6.3. Data Generation and Experimental Setup

Figure 6.7: Examples of simulated conductivity images and corresponding mask images. For each pair, the left is the binary mask image, and the right is the conductivity image. Green circle denotes the boundary of the sensing region.

Figure 6.8: The composition of the final augmented dataset.

Mask images for training and evaluation are also generated in simulation by a simple approach of assigning number one to pixels where there are objects and number zero to the rest of the pixels. Four examples of the simulated conductivity images and corresponding binary mask images are illustrated in Fig. 6.7.

Based on the settings above, we built a dataset with 19,177 samples. Each sample comprises a frame of voltage measurements, a ground-truth conductivity image, and a mask image. There are 4,691 1-object samples, 4,736 2-object samples, 4,936 3-object samples and 4,814 4-object samples. In order to maintain the data balance in training and evaluation, we randomly select 10% samples as the test set and 10% samples from the remaining data as the validation set for each type of data. The rest will serve as the training set. As a result, we have 15,537 samples for training, 1,724 samples for validation, and 1,916 samples for testing.
Moreover, to improve the robustness of our model, additive Gaussian noise is added to the voltage measurements to augment the original dataset. For each type of data (i.e. 1-object samples, 2-object samples, 3-object samples, and 4-object samples), we separately add noise with the Signal-to-Noise Ratio (SNR) of 50 dB and 40 dB to half of the data in the training and validation set. For the test data, the noise with the SNR of 50 dB, 40 dB and 30 dB is separately added to the entire test set. Fig. 6.8 displays the composition of the final dataset adopted to train and evaluate our model.

6.3.2 Dual-modal Imaging System Setup

The dual-modal sensor is connected to the in-house developed EIT system (Y. Yang & Jia, 2017b) to collect real-world experimental data. The frame rate of the system is set as 48 fps and its highest SNR is 82.82 dB (Y. Yang & Jia, 2017b). In experiments, the frequency of the injected current is set as 10 kHz. In addition, the view field of the digital microscope and the sensing area of the impedance sensor coincide precisely.

6.3.3 Network Training

The MSFCF-Net is implemented using Pytorch, trained and tested on a workstation with a GeForce RTX 2070 Super. AdamW (Loshchilov & Hutter, 2018) is employed for optimization. We use the whole training set (31,074 samples) and the whole validation set (3,448 samples) to train MSFCF-Net. Early stopping is adopted to mitigate overfitting. The hyperparameters are set as follows: the learning rate is $10^{-4}$ and the penalty parameter $\lambda$ is set as $10^{-6}$; the maximum number of training epoch is 200 and the batch size of each update is 120; the tolerance is set as 10 epochs for early stopping. Finally, the training process is stopped at epoch 90 and the training time is 86.70 minutes. The model with minimum validation loss is selected as the final model.

6.4 Results and Discussion

The proposed method is evaluated by numerical simulation and MCF-7 cell spheroids experiments. The performance of MSFCF-Net is compared with other widely used single-modal-based EIT image reconstruction algorithms, i.e., Gaussian-Laplace regularization (TReg-GL) (Y. Yang et al., 2014) and Sparse Bayesian Learning (SBL) (S. Liu et al., 2018), and a dual-modal based image reconstruction algorithm using Cross-Gradient regularization (CG) (Z. Li et al., 2019). In this work, the mask image replaces the CT image in (Z. Li et al., 2019) as the assisted image in both simulation and real experiments. We also compare with the recently proposed end-to-end deep learning model FC-UNet (Chen et al., 2020) and the single-modal version of MSFCF-Net (named S-MSFCF-Net). FC-UNet was originally designed for pixel-level classification for EIT images. As we treat the conductivity distribution prediction as a
6.4. Results and Discussion

Table 6.1: Quantitative metrics for comparing different algorithms on the test set.

<table>
<thead>
<tr>
<th>Algorithms</th>
<th>Noise-free</th>
<th>50 dB</th>
<th>40 dB</th>
<th>30 dB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M-RIE</td>
<td>M-MSSIM</td>
<td>M-RIE</td>
<td>M-MSSIM</td>
</tr>
<tr>
<td>TReg-GL</td>
<td>0.9481</td>
<td>0.3879</td>
<td>0.9481</td>
<td>0.3875</td>
</tr>
<tr>
<td>SBL</td>
<td>1.5527</td>
<td>0.7553</td>
<td>1.5517</td>
<td>0.7546</td>
</tr>
<tr>
<td>CG</td>
<td>0.9278</td>
<td>0.4035</td>
<td>0.9279</td>
<td>0.4028</td>
</tr>
<tr>
<td>FC-UNet</td>
<td>0.4946</td>
<td>0.8708</td>
<td>0.4949</td>
<td>0.8707</td>
</tr>
<tr>
<td>S-MSFCF-Net</td>
<td>0.5150</td>
<td>0.8453</td>
<td>0.5151</td>
<td>0.8453</td>
</tr>
<tr>
<td>MSFCF-Net</td>
<td>0.3715</td>
<td>0.9387</td>
<td>0.3715</td>
<td>0.9387</td>
</tr>
</tbody>
</table>

Table 6.2: Comparison of different algorithms on different types of samples.

<table>
<thead>
<tr>
<th>Algorithms</th>
<th>1-Object</th>
<th>2-Object</th>
<th>3-Object</th>
<th>4-Object</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M-RIE</td>
<td>M-MSSIM</td>
<td>M-RIE</td>
<td>M-MSSIM</td>
</tr>
<tr>
<td>FC-UNet</td>
<td>0.2334</td>
<td>0.9817</td>
<td>0.4803</td>
<td>0.9096</td>
</tr>
<tr>
<td>S-MSFCF-Net</td>
<td>0.2780</td>
<td>0.9644</td>
<td>0.4742</td>
<td>0.8868</td>
</tr>
<tr>
<td>MSFCF-Net</td>
<td>0.0626</td>
<td>0.9920</td>
<td>0.4043</td>
<td>0.9478</td>
</tr>
</tbody>
</table>

regression problem, to make a fair comparison, we remove the activation function in the output layer of the FC-UNet. For S-MSFCF-Net, we remove the BN-M and DMFF modules while the MSFF modules fuse different scales of feature maps from BN-V. Except for the tolerance of early stopping, FC-UNet and S-MSFCF-Net are also trained with the same loss function and settings as MSFCF-Net. The early stopping tolerance for FC-UNet and S-MSFCF-Net is set as 20 because it is beneficial to promote their convergence. It should be noted that in all reconstructed EIT images, the magnitude of each pixel denotes the quantity in (6.10).

6.4.1 Numerical Simulation

In simulation study, RIE and MSSIM (Z. Wang et al., 2004) are the metrics for the evaluation of single image quality. The definitions of the two metrics are stated in (3.27) and (3.28), respectively. Another two numerical metrics that evaluate the performance on the whole dataset level are the mean RIE (M-RIE) and the mean MSSIM (M-MSSIM). During the evaluation process, we calculate RIE and MSSIM for each image in the test set and then average all values.

Table 6.1 illustrates the quantitative evaluation results at different SNR levels on the test set. It is evident that the metrics of MSFCF-Net are superior to other given algorithms, indicating the robustness and effectiveness of the proposed dual-modal framework. Deep learning-based methods all show better voltage noise-resistance capability than conventional model-based algorithms. Especially, the M-MSSIM of deep learning models maintains a similar level with the decrease of SNR. Table 6.2 compares the metrics of deep learning models on different types of samples with the SNR = 50 dB. As reconstructing multi-object and multi-level conductivity
distribution is much more challenging, the metrics on 2-object samples have a big drop than those on 1-object samples for all deep learning models. For a specific type of sample, it is evident that the performance of MSFCF-Net is much better than the other two. Especially, though S-MSFCF-Net only removes the mask image-related structures from MSFCF-Net, it still cannot reach the performance of MSFCF-Net. The reason is that: single-modal deep learning models will take the duty on both position and structure prediction and conductivity value prediction. But the proposed dual modal deep learning model in essence utilizes more structural information; thus, better conductivity prediction can be expected.

Fig. 6.9 and Fig. 6.10 compare five representative phantoms reconstructed from test data with SNR = 50 dB. GT denotes the ground truth image. The left column under each algorithm is the reconstructed EIT image and the right one is the error image which is the absolute difference between the reconstructed image and the ground truth image. Mask images (from left to right) corresponding to samples in Fig. 6.9 and Fig. 6.10 (from top to bottom) are
6.4. Results and Discussion

Figure 6.10: Image reconstruction results of learning-based algorithms on five representative samples (Left column: Reconstruction; Right column: Error image).

Figure 6.11: Mask images corresponding to samples in Fig. 6.9 and Fig. 6.10.

illustrated in Fig. 6.11. Although both TReg-GL and SBL can predict the position of objects, the shape and conductivity values are always inaccurate (see their error images, RIE and MSSIM). For CG, the reconstructed images are very similar to images by TReg-GL and the quality of images is not improved noticeably according to their error images and numerical metrics. However, if the image generated by CG is zoomed, it is obvious that clear boundaries of objects are visible, which is exactly the result of introducing Cross-Gradient regularization. Thus, the Cross-Gradient regularization can only augment the object boundaries based on the
assisted image while it cannot essentially improve the EIT image quality. For deep learning-based approaches, FC-UNet and S-MSFCF-Net can generate more accurate position, shape and conductivity values, but the errors are still more significant than those of the MSFCF-Net. Only MSFCF-Net can reconstruct the best EIT images among the given algorithms with the most accurate position, shape, and conductivity values. Especially, the results of the second row and the fourth row indicate that the MSFCF-Net can reconstruct images correctly that the other two networks cannot do, which benefits from introducing another imaging modality.

In this study, all model-based algorithms are based on the linearized EIT forward model introducing intrinsic model error. Therefore, it is difficult for these linearized model-based methods to predict accurate results, which may lead to under or over-estimation of conductivity values. Deep-learning-based methods directly fit the non-linear mapping of the EIT inverse problem, which can theoretically generate more accurate predictions. However, the performance of learning-based methods highly depends on the quality of training datasets and training strategies. Thus, we produce a large dataset and carefully train the proposed network to mitigate the adverse effect caused by such limitations.

In many tissue engineering applications, cells are cultured within the scaffold, and monitoring of cell growth is vital to the process (Y. Yang et al., 2019). Cell growth at different stages within the scaffold will decrease the conductivity of various levels, which can be mapped by EIT (Wu, Zhou, et al., 2018). To further demonstrate the effectiveness of the proposed framework, we simulated the imaging of cell growth within bio-scaffolds (Wu, Zhou, et al., 2018; Y. Yang et al., 2019) by using EIT. We modeled a regular-shape scaffold, a quasi-2D EIT sensor with 16
electrodes, and a cell culture model with two cell clusters (see Fig. 6.12). The modeled sensor
has the same dimension as the real sensor in Fig. 6.2. The height and diameter of the scaffold
are 1.2 mm and 3 mm, respectively. The background conductivity is set as 0.05 S/m and the
conductivity of the scaffold material is set as $10^{-8}$ S/m. The cells are modelled as evenly
distributed in the space among scaffolds. We modelled two scenarios. The first contains one
cell cluster and the conductivity of the cells cluster is set as 0.025 S/m. The second has two
cell clusters to simulate cell growth at two different stages. The conductivities in cell cluster
1 and cell cluster 2 are set as 0.02 S/m and 0.04 S/m, respectively. In these cases, the
reference conductivity distribution for the first scenario is the homogeneous medium whose
conductivity is 0.05 S/m with a scaffold and the reference conductivity distribution for the
second scenario is the same homogeneous medium including two scaffolds. Therefore, only
the cell’s conductivity contributes to the predicted conductivity variation, which is also indicated
in (Y. Yang et al., 2019).

Fig. 6.13 gives the image reconstruction results under the settings described in the last
paragraph. By using the proposed approach, we could obtain reconstruction images with
RIE lower than 0.22 and SSIM larger than 0.96. The results show strong evidence that the
proposed framework can generate accurate conductivity distribution under a different setting.
It also presents good generalization ability when dealing with the challenging scenario of
scaffold-based cell culturing imaging.

It is worth further discussing the generalization ability and the limitations of our method. In
practical applications of the proposed method, inaccurate mask images may be generated due
to many factors, such as an unideal guidance image processing algorithm or noisy guidance
image. To assess the robustness of the proposed method when encountering an inaccurate
mask image, Fig. 6.14 selects the first and fifth samples in Fig. 6.9 (or Fig. 6.10) for further
Figure 6.14: Image reconstruction results based on perturbed mask images.

Two different random perturbations are applied to the mask images of each sample, which are shown in the first column of the table. Each result occupying one row contains three images, i.e. the input mask image, the predicted EIT image and the error image from left to right. Observing the error images, the conductivity value can still be predicted accurately except for the pixels on the boundary while losing some structural information. Compared with the results generated by MSFCF-Net in Fig. 6.10, although the quality of the image based on the perturbed mask image is lower than the quality of that based on the accurate mask.
6.4. Results and Discussion

Figure 6.15: MSFCF-Net image reconstruction results of six phantoms (a)-(f) based on the data which do not satisfy our dataset construction criteria. From left to right, each column represents the ground truth, reconstructed EIT image and error image, respectively. Red numbers in (a) and (b) denote the relative conductivity change, i.e. $I^{eit}$ in (6.10), at the sampling points in the images. The size of the inclusions in the yellow circles in (c) is smaller than $0.07d$. The inclusions in the rose circles in (e) are the ones that are well-predicted. The inclusion in the blue circle in (f) means this one is not identified by the mask image.

R$\text{IE} = 0.1320$, MSSIM = 0.9593

R$\text{IE} = 0.2010$, MSSIM = 0.9916

R$\text{IE} = 0.4759$, MSSIM = 0.9066

R$\text{IE} = 0.2800$, MSSIM = 0.9136

R$\text{IE} = 0.0991$, MSSIM = 0.9785

R$\text{IE} = 1.0282$, MSSIM = 0.8552

(see RIE and MSSIM), the quality of these images is still much better than the quality of images generated by the model-based algorithms. This analysis implies that, in real-world experiments, we can acquire a quantitatively meaningful EIT image even if the guidance image processing algorithm cannot generate a very accurate mask image.

In Fig. 6.15, we also discuss another five situations which are inconsistent with our criteria of data generation but may occur in real applications. Some of them are extreme cases. There are six pairs of results, and each pair of results includes three images, i.e. the ground truth, reconstructed EIT image and error image. Results in Fig. 6.15 (a) to (e) are based on the accurate mask images. Fig. 6.15 (a) and (b) display the results when the conductivity of one inclusion is close to the background conductivity. It is clear that our method can still recover the conductivity contrasts though the error of conductivity prediction exists. Fig. 6.15 (c) illustrates the result under the situation that the size of two inclusions (around $0.05d$) is smaller than $0.07d$, and Fig. 6.15 (d) shows the result under the situation that the size of the inclusion (around $0.35d$) is larger than $0.3d$. The results demonstrate that our method can still reconstruct the conductivity well if the sizes of certain inclusions never appear in our training set. Fig. 6.15 (e) is the result of imaging five inclusions by our approach. This type of sample does not appear
in the training set neither. It is obvious that the prediction error is much larger. However, the conductivity of three inclusions can still be approximately predicted, which can be indicated by the error image. Fig. 6.15 (f) shows the result based on the assumption that the mask image fails to identify the inclusion in the blue circle, which means the pixel values of that inclusion in the mask image are all zeros, while the mask image provides an accurate profile for the other inclusion. This extreme scenario may occur when the optical sensor has no response on some inclusions, or the guidance image processing algorithm is imperfect. In this case, only the inclusion identified by the mask image appears in the reconstructed EIT image, indicating that identifying objects in the mask image is essential in our approach. This prerequisite is acceptable as our method conducts dual-modal imaging. To summarize, the proposed dual-modal imaging approach can generate satisfactory images if the inclusions can be correctly recognized by the optical image and the guidance image processing algorithm. Our method demonstrates generalization ability and robustness when encountering voltage noise, mask image perturbation and some situations not satisfying our data generation criteria.

6.4.2 Cell Experiments

The performance of the proposed framework is further evaluated on data collected from real-world experiments (see Fig. 6.16). The imaging target is MCF-7 cell spheroids (diameter \( \approx 2 \) mm). The rightest column is the mask image generated from the guidance image processing algorithms stated in Subsection 6.2.2. The threshold values \( \beta \) in (6.4) for the three guidance images (from top to bottom) are set as 0.66, 0.45, and 0.5 respectively based on a series of trials. The \( 3 \times 3 \) kernel is adopted in the next two morphological operations for all cases.

In Fig. 6.16, the red dashed line denotes the location of the cell spheroids. For conventional model-based single-modal and dual-modal algorithms, the cell spheroid structure is lost, and the reconstructed images contain too much unmeaningful information in the background, although they can locate the position of cell spheroids. As discussed in Subsection 6.4.1,
the augmented object boundary is visible in images reconstructed by CG while the quality of these images is not essentially improved in the visual. Although the model-based algorithms are defeated in terms of shape preservation and noise reduction, TReg-GL and CG generate acceptable conductivity estimation (for TReg-GL, \( \sim 0.30 \) for the first and third phantom, \( \sim 0.25 \) for the second phantom; for CG, \( \sim 0.22 \) for all phantoms) according to the estimated relative conductivity change of MCF-7 cells (\( \sim 0.39 \)) using the simplified single-shell model and computing method in (Cottet et al., 2019). The deep learning models outperform in artifacts suppression. The MSFCF-Net could generate the most accurate shape and acceptable conductivity change (\( \sim 0.25 \) for the first phantom, \( \sim 0.12 \) for the second phantom, and \( \sim 0.30 \) for the third phantom) according to the estimated conductivity change of MCF-7 cells. The reconstructed conductivity change of the second phantom deviates more from the reference value, possibly due to the more considerable measurement noise than the other two phantoms. It is also worth noting that such a theoretical approximation based on several assumptions might not be accurate. In the future, a possible method to better quantify the experiment results is to use hydrogel as phantoms, whose shape and conductivity value could be better controlled.

6.5 Summary

In this Chapter, we proposed an impedance-optical dual-modal imaging framework for 3D cell culture imaging. We combined optical imaging with EIT to tackle the low image quality issue of EIT. We also developed a learning-based approach to fuse the dual-modal information and reconstruct high-quality conductivity images. The results of simulation data and real-world data on MCF-7 cell spheroids demonstrate that the proposed framework could generate a more accurate estimation of conductivity distribution, which implies the possibility of quantitative imaging for EIT in tissue engineering. Future research will deal with the situation when the structure of the object in the mask image suffers more severe perturbation and develop more advanced image processing algorithms to generalize the method to other optical imaging approaches for tissue engineering, e.g., optical coherence tomography.
Chapter 7

Conclusions and Future Work

7.1 Conclusions

Electrical Impedance Tomography (EIT) is a widely investigated functional imaging modality that aims to reveal the conductivity distribution of the sensing region through boundary voltage measurements. Due to its portability, non-intrusiveness, lack of radiation, and high temporal resolution, EIT stands out as an ideal bedside imaging technique for real-time and long-term imaging in various biological and medical applications. However, the low spatial resolution, which leads to low image quality, hinders quantitative analysis and broader application of EIT in tissue engineering. This thesis makes a concerted effort to address the issue of low quality in EIT by introducing an EIT-incorporated multi-modal approach for tissue engineering. The detailed work and specific contributions of this thesis are summarized as follows.

The principles of EIT, several published EIT-incorporated multi-modal systems, single-modal and multi-modal image reconstruction algorithms, and the applications of EIT in tissue engineering were initially reviewed. This review offers readers an initial impression of what EIT is and how it operates. Additionally, the review uncovers the limitations of single-modal EIT imaging and underscores the importance of investigating the EIT-incorporated multi-modal approach for function-structure tissue imaging.

Expanding upon the general multi-modal imaging framework delineated in Chapter 1 (please refer to Fig. 1.1), a multi-modal model-based image reconstruction algorithm, named Image-Guided Group Sparsity (IGGS), was introduced. IGGS incorporates structural information from microscopic images into EIT image reconstruction by utilizing non-overlapping group sparsity regularization. The grouping rules have been meticulously designed and are derived from the semantic segmentation of the microscopic images. Due to the promotion of sparsity among groups, inherent in group sparsity, the algorithm has shown robust noise resistance. Furthermore, through simulations and experiments, IGGS has consistently outperformed existing algorithms in terms of conductivity differentiation, structural preservation, and suppression of background artifacts. As a result, this initial example effectively demonstrates the advantages of the multi-modal approach.
IGGS necessitates semantic segmentation, introducing additional computational costs. An alternative multi-modal approach, named the Kernel Method, was proposed for EIT image reconstruction. The Kernel Method is a segmentation-free algorithm, thereby eliminating the need for image segmentation and reducing computational expenses. This method incorporates structural information from an auxiliary high-resolution image into the EIT inversion process through the kernel matrix. In comparison to the existing state-of-the-art algorithms, the proposed kernel method generates superior EIT images in challenging simulation and experimental scenarios. It also offers the advantage of suppressing interference from imaging-irrelevant objects in the auxiliary image. Nevertheless, since kernel-based regularization lacks sparsity priors, complete suppression of background artifacts is not achieved. Nonetheless, the Kernel Method still illustrates the benefits of incorporating additional information, particularly the enhanced ability to differentiate various conductivity values and preserve target structures.

Addressing drawbacks in IGGS and the Kernel Method, the new OGLL algorithm integrates their strengths, combining IGGS’s sparsity promotion with the Kernel Method’s segmentation-free approach. Simulations and experiments confirm OGLL’s effective background artifact suppression. By employing overlapping groups and categorizing conductivity changes based on local characteristics of the auxiliary image, OGLL improves structure preservation, background artifact suppression, and conductivity contrast differentiation over existing algorithms. Notably, OGLL’s group overlapping eliminates the need for finely crafted grouping rules, differing from non-overlapping grouping. Overall, OGLL demonstrates that the multi-modal approach can achieve superior image quality compared to single-modal methods.

Finally, this thesis explores deep learning for multi-modal image reconstruction in 3D cell culture, presenting a novel impedance-optical dual-modal imaging framework applicable to diverse tissue engineering contexts. Comprising an impedance-optical sensor, a guided image processing algorithm, and the Multi-Scale Feature Cross Fusion Network (MSFCF-Net), the framework effectively fuses EIT measurements and binary mask images from guidance processing to enhance conductivity imaging. Validation via simulations and MCF-7 cell imaging experiments demonstrate significant image quality improvements. This highlights the potential of impedance-optical joint imaging for simultaneous structural and functional insights into tissue-level targets.

In summary, the work presented in this thesis bridges the research gap in multi-modal impedance imaging. The exploration of model-based and learning-based imaging approaches, combined with their integration into the self-developed EIT system, has been conducted. The outcomes obtained in this thesis have the potential to elevate EIT-incorporated multi-modal imaging as a robust, high-quality, and intelligent imaging technique for tissue engineering applications. This advancement may also serve to accelerate breakthroughs in the field of biomedical engineering.
7.2 Future Work

While this thesis has achieved progress in 3D cell culture imaging through the developed multi-modal techniques, further investigation is still required to advance this work in the following aspects:

- **Algorithm Extension**: The algorithms proposed in this thesis, i.e., IGGS, the Kernel Method, OGLL, and MSFCF-Net, can be seamlessly extended into 3D image reconstruction. When combined with 3D sensors, a wider range of complex behaviors and phenomena in 3D tissues can be comprehensively explored.

- **EIT Sensor Design and Measurement Strategy Optimization**: Sensor design encompasses sensor material selection or synthesis, sensor structure design, and sensor dimension selection. These aspects typically have an impact on signal quality, subsequently influencing the overall performance of the EIT system. Therefore, designing an advanced EIT sensor is of great significance. In particular, within the field of tissue engineering, sensor miniaturization is not only necessary but also presents a significant challenge in sensor design, demanding dedicated efforts. Furthermore, measurement strategies play a crucial role in determining the amount of information collected in the signal, which, in turn, affects the quality of the reconstructed EIT image. An effective measurement strategy can enhance EIT sensitivity and capture as much useful information as possible.

- **Auxiliary Modality Selection and Information Fusion**: Auxiliary modalities can offer additional information to enhance EIT invertibility. Hence, aside from the auxiliary modality utilized in this thesis, the selection of other suitable auxiliary imaging modalities is pivotal for multi-modal imaging in a specific application. Moreover, considering the unique characteristics of the application and the multi-modal imaging setup, information fusion algorithms should be thoroughly explored and thoughtfully designed.

- **Image Reconstruction Capturing Frequency Correlation**: In this thesis, all algorithms only utilize a single frequency for time-difference imaging. In tissue engineering applications, imaging targets (cells and tissues) are too small (up to several microns) to perform time-difference imaging because time-difference imaging usually requires homogeneous conductivity reference. Although the reference conductivity distribution can be selected at any time, the structural information tends to be lost if the reference conductivity distribution is inhomogeneous. Consequently, frequency difference imaging emerges as a viable alternative. However, there is limited research on frequency-difference imaging. Therefore, further investigation is required to effectively capture the correlation of the same imaging targets across different frequencies.
7.2. Future Work

- **Image Reconstruction Incorporating Spatiotemporal Correlation:** Monitoring 3D cell cultures necessitates dynamic imaging, resulting in time-series measurement data. Algorithms in this thesis only rely on single-frame data to reconstruct EIT images, and the images reconstructed from multiple frames are treated as independent. These methods overlook the temporal correlation of the conductivity distribution. Furthermore, the reconstructed images are vulnerable to measurement noise, which can disrupt the temporal correlation between images reconstructed at different time points. Consequently, there is a need for extensive exploration of regularization techniques that incorporate spatiotemporal correlations within the conductivity distribution to enhance EIT image quality and algorithm stability.

- **3D Image Representation:** Traditionally, images are typically represented using pixels/voxels, and this type of image representation is also employed in this thesis. However, for 3D image reconstruction, such a representation demands a substantial amount of computational memory, which significantly inflates financial costs and prolongs the training process. Consequently, it is imperative to investigate dedicated and efficient image representations for 3D imaging reconstruction to address the issues related to financial expenses and memory consumption.

- **Benchmarking on Complex Biological Samples:** In this thesis, the phantoms consist of either simple geometrical objects or cell spheroids. Additionally, we exclusively perform static imaging. In the future, there is potential to explore real-time imaging of cell status. The proposed multi-modal methods are anticipated to undergo a comprehensive evaluation on intricate biological samples, such as organoids, further pushing the boundaries of application for this technique.


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REFERENCE


