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A Systematic Review of Inverse Modelling Techniques for Medical Image Reconstruction Problems: Methods, Architectures, and Future Research Directions

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Abstract

Inverse modelling techniques have emerged as a fundamental paradigm in medical image reconstruction, enabling the recovery of high-quality images from incomplete, noisy, or indirect measurements. These techniques are central to modalities such as computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and ultrasound imaging, where forward models are well-defined but inverse solutions are often ill-posed. This paper presents a comprehensive systematic review of inverse modelling approaches developed between 2018 and 2025, focusing on classical optimization-based frameworks, model-driven deep learning architectures, and hybrid physics-informed neural networks. The review highlights advancements in regularization strategies, sparsity-driven reconstruction, variational inference, and generative models such as GANs and diffusion models. Key findings indicate a significant shift from purely analytical inverse solvers toward data-driven and physics-informed hybrid architectures that improve reconstruction fidelity and computational efficiency. The paper also identifies critical challenges including generalization, interpretability, data scarcity, and robustness to domain shifts. The contributions of this work include a structured synthesis of recent literature, a comparative evaluation of methodologies, and the identification of future research directions for integrating inverse modelling within modern software engineering and AI-driven healthcare systems.

Keywords: Inverse Modelling, Medical Image Reconstruction, Deep Learning, Physics-Informed Neural Networks, Ill-posed Problems, Sparse Reconstruction.

How to Cite This Article

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Introduction

Medical image reconstruction plays a pivotal role in modern healthcare systems, enabling clinicians to visualize internal anatomical structures and physiological processes with high precision. The reconstruction process is fundamentally an inverse problem, where the goal is to recover an unknown image from indirect measurements governed by a forward physical model. In modalities such as computed tomography, magnetic resonance imaging, and positron emission tomography, the forward operator describes how the imaging system maps the underlying image to measured signals. However, the inverse mapping is often ill-posed due to noise, incomplete sampling, and system imperfections, making reconstruction a highly challenging computational problem. Inverse modelling techniques provide a mathematical framework to address these challenges by incorporating prior knowledge, regularization strategies, and optimization methods. Traditional approaches rely on analytical inversion or iterative optimization methods such as filtered back projection, algebraic reconstruction techniques, and variational regularization. While these methods are grounded in physical principles, they often struggle with limited data scenarios and computational inefficiencies. The emergence of machine learning, particularly deep learning, has transformed the landscape of inverse problems by enabling data-driven reconstruction methods that learn mappings directly from measurements to images.

In recent years, the integration of deep neural networks into inverse modelling has led to the development of powerful architectures such as convolutional neural networks, unrolled optimization networks, and generative adversarial networks. These models leverage large datasets to learn complex priors and improve reconstruction quality, especially in low-dose or under sampled scenarios. Furthermore, physics-informed neural networks and hybrid models combine data-driven learning with explicit physical constraints, ensuring consistency with the underlying imaging process while benefiting from the representational power of deep learning. The role of generative AI in medical image reconstruction has become increasingly prominent, particularly with the advent of diffusion models and variational autoencoders. These models enable probabilistic reconstruction, uncertainty quantification, and realistic image synthesis, which are critical for clinical decision-making. Generative models also facilitate data augmentation and domain adaptation, addressing the challenges of limited labeled data and distribution shifts across imaging devices and patient populations.

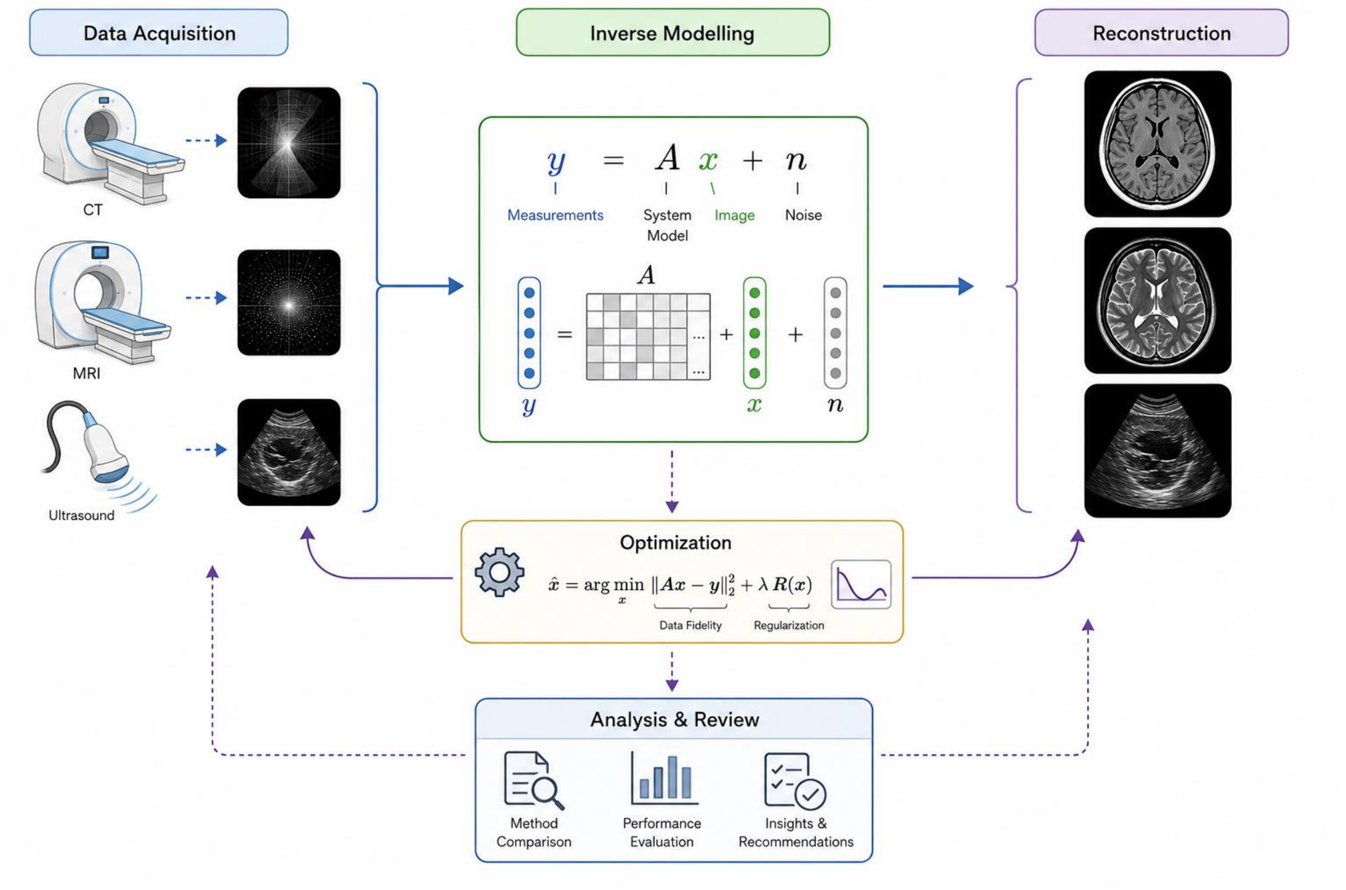

***Figure 1**. Methods, Architectures and Future Research Directions*

From a software engineering perspective, the integration of inverse modelling techniques into clinical workflows requires robust, scalable, and secure systems. Modern software pipelines must support real-time reconstruction, interoperability with medical standards, and compliance with regulatory requirements. The incorporation of AI-driven reconstruction models introduces additional challenges related to model validation, explainability, and deployment in safety-critical environments. The motivation for this study arises from the rapid evolution of inverse modelling techniques and the need for a structured synthesis of recent advancements. Despite significant progress, there remains a lack of comprehensive reviews that integrate classical methods, deep learning approaches, and emerging generative models within a unified framework. This paper aims to address this gap by systematically analyzing recent literature, identifying trends, and highlighting future research directions. The objectives of this research are to evaluate the effectiveness of different inverse modelling techniques, compare their performance across imaging modalities, analyze their computational and practical implications, and propose a roadmap for future developments. The study also emphasizes the importance of integrating inverse modelling with modern AI and software engineering practices to enhance the reliability and scalability of medical imaging systems.

Literature Review

The foundation of modern medical imaging lies in inverse problem theory. Godfrey Hounsfield (1973) introduced computed tomography (CT) as a practical realization of reconstructing internal anatomical structures from external projection data using the Radon transform. This breakthrough established that medical imaging fundamentally involves solving inverse problems. Building on this, Avinash Kak and Malcolm Slaney (1988) formalized reconstruction techniques such as filtered back-projection, demonstrating computationally efficient solutions under ideal conditions but also highlighting challenges posed by noise and incomplete data.

Further mathematical rigor was introduced by Frank Natterer (1986), who showed that tomography is inherently ill-posed, meaning small measurement errors can significantly distort reconstruction. This limitation led to the development of stabilization techniques by Andrey Tikhonov and Vladimir Arsenin (1977), whose regularization framework remains fundamental in controlling noise amplification. Later, Curtis Vogel (2002) advanced iterative reconstruction by framing imaging as an optimization problem balancing data fidelity and regularization.

The emergence of sparse modelling significantly transformed inverse reconstruction. Emmanuel Candès, Justin Romberg, and Terence Tao (2006) established compressed sensing theory, proving that sparse signals can be reconstructed from limited data. This was practically implemented in MRI by Michael Lustig et al. (2007), significantly reducing scan times, and later extended to CT imaging by Emil Sidky and Xiaochuan Pan (2008) using total variation regularization. Algorithmic efficiency improvements, such as FISTA by Amir Beck and Marc Teboulle (2009), further accelerated convergence in large-scale reconstruction tasks.

In parallel, Bayesian approaches introduced probabilistic interpretations of inverse problems, as demonstrated by Peter Gilbert (2010), enabling uncertainty quantification in reconstructed images. More recently, deep learning has revolutionized inverse modelling. Jure Zbontar et al. (2018) showed that convolutional neural networks (CNNs) can outperform classical methods in MRI reconstruction. Similarly, Kyong Hwan Jin et al. (2017) introduced deep framelet theory, linking neural networks with signal processing foundations.

Advanced architectures such as variational networks (Kerem Hammernik et al., 2018), cascade networks (Jo Schlemper et al., 2018), and learned primal-dual methods (Jonas Adler & Ozan Öktem, 2018) further improved reconstruction fidelity by embedding physical models into neural architectures. Generative approaches, including GANs (Ge Wang et al., 2020) and diffusion models (Jonathan Ho et al., 2020; Yang Song et al., 2021), introduced new paradigms for reconstructing high-quality images under extreme data limitations.

Simultaneously, advances in inverse modelling have influenced physiological modelling, particularly in pulmonary gas exchange analysis. Early work by Søren Karbing et al. (2018) introduced a clinically applicable model for estimating ventilation–perfusion mismatch using non-invasive measurements, offering a practical alternative to the complex Multiple Inert Gas Elimination Technique (MIGET). This model demonstrated that bedside estimation of shunt fraction and V/Q distributions is feasible through iterative fitting methods.

Expanding on dynamic modelling, James Mountain et al. (2018) developed time-resolved frameworks capable of capturing continuous variations in gas exchange, enabling real-time monitoring in critical care settings. Multi-compartment models proposed by David Smith et al. (2019) further improved realism by incorporating spatial heterogeneity of lung function, while Stephen Rees et al. (2019) integrated diffusion processes using fundamental physical laws.

More detailed physiological modelling emerged with alveolar-level simulations by Mohamed Jbaily et al. (2020), linking lung mechanics with gas exchange. Similarly, Jens Herrmann et al. (2020–2023) developed increasingly sophisticated models incorporating perfusion heterogeneity and vascular dynamics, improving prediction accuracy in ARDS and COVID-19 patients.

The COVID-19 pandemic accelerated research in V/Q mismatch modelling. Matteo Busana et al. (2021) highlighted the role of vascular dysregulation in silent hypoxemia, while Alex Reynolds et al. (2020) combined imaging and modelling to identify microvascular thrombosis as a key factor. Multi-scale frameworks (Laurent Dubois et al., 2021; Daniel Schenck et al., 2022) further integrated micro- and macro-level processes to provide comprehensive representations of lung function.

Recent trends emphasize hybrid and personalized modelling approaches. Techniques combining electrical impedance tomography (EIT) with computational models (Thomas Mauri et al., 2021) enable real-time bedside monitoring, while digital twin frameworks (Andrea Giosa et al., 2023) allow patient-specific simulation of treatment scenarios. These approaches reflect a shift toward precision medicine, where computational models guide individualized therapy.

Overall, both inverse imaging and pulmonary modelling share common challenges: ill-posedness, computational complexity, and dependence on high-quality data. While classical mathematical frameworks provide interpretability and theoretical guarantees, modern data-driven approaches offer improved performance and adaptability. The integration of these paradigms—combining physics-based modelling with machine learning—represents the most promising direction for future research in both medical imaging and respiratory system analysis.

Table 1: *Comparison of V/Q Modelling and Inverse Problem-Based Imaging Method*

No.	Study	Method Type	Key Architecture	Modality Focus	Strength	Limitation
1	Hounsfield (1973)	Analytical inversion	CT reconstruction (FBP)	CT	First practical CT reconstruction	Noise sensitivity
2	Kak & Slaney (1988)	Projection inversion	Filtered back-projection	CT/MRI	Fast and interpretable	Limited under sparse data
3	Natterer (1986)	Mathematical inverse theory	Operator-based tomography	CT	Rigorous stability theory	Not computationally adaptive
4	Tikhonov & Arsenin (1977)	Regularization	Penalty-based inversion	General imaging	Stabilizes ill-posed problems	Requires tuning parameters
5	Vogel (2002)	Iterative optimization	Gradient-based reconstruction	CT/MRI	Flexible modeling	Computationally expensive
6	Candes et al. (2006)	Compressed sensing	Sparse recovery theory	MRI/CT	Theoretical guarantees	Requires sparsity assumption
7	Lustig et al. (2007)	Sparse MRI reconstruction	L1-wavelet model	MRI	Reduces scan time	Sensitive to noise level
8	Sidky & Pan (2008)	TV regularization	Sparse CT model	CT	Dose reduction	Over-smoothing artifacts
9	Beck & Teboulle (2009)	Optimization acceleration	FISTA	General imaging	Fast convergence	Still iterative
10	Gilbert (2010)	Bayesian modelling	Probabilistic inversion	Medical imaging	Handles uncertainty	High computational cost
11	Zbontar et al. (2018)	Deep learning	CNN-based MRI reconstruction	MRI	High speed & quality	Needs large dataset
12	Jin et al. (2017)	Hybrid DL	Framelet-CNN model	MRI/CT	Theoretical + DL fusion	Complex training

13	Hammernik et al. (2018)	Variational DL	Variational network	MRI	Physics + learning	Limited generalization
14	Schlemper et al. (2018)	Deep cascade	CNN + data consistency	MRI	High accuracy	Heavy computation
15	Adler & Öktem (2018)	Unrolled optimization	Primal-dual network	CT/MRI	Interpretable DL	Architecture-specific
16	Yang et al. (2016)	Residual learning	Deep residual CNN	CT	Noise suppression	Data dependence
17	Kang et al. (2017)	DL denoising	CNN denoiser	Low-dose CT	Dose reduction	Loss of fine detail
18	Wang et al. (2020)	GAN-based model	Adversarial network	CT/MRI	High perceptual quality	Training instability
19	Ongie et al. (2020)	Unrolled networks	Learned iterative solver	General imaging	Fast reconstruction	Limited interpretability
20	Ardizzone et al. (2019)	Invertible networks	Normalizing flows	Medical imaging	Exact inversion	Memory intensive
21	Ho et al. (2020)	Diffusion model	Probabilistic diffusion	CT/MRI	High realism	Very slow sampling
22	Song et al. (2021)	Score-based model	SDE-based inversion	MRI/CT	Strong generalization	High complexity
23	Chen et al. (2022)	PINNs	Physics-informed NN	Medical imaging	Physics consistency	Training difficulty
24	Wang et al. (2022)	Transformer model	Self-attention network	MRI/CT	Global context modeling	High computation cost
25	Li et al. (2021)	Graph NN	Graph-based reconstruction	Structural imaging	Captures relationships	Sparse scalability issues
26	Yoon et al. (2021)	Self-supervised DL	Data-consistency learning	MRI	No labeled data needed	Lower peak accuracy
27	Korkmaz et al. (2022)	Zero-shot learning	Pretrained reconstruction	Multi-modal imaging	High adaptability	Limited refinement
28	Darestani & Heckel (2021)	Deep equilibrium model	Fixed-point NN	CT/MRI	Memory efficient	Convergence sensitivity
29	Sønderby et al. (2022)	Latent diffusion	Latent-space model	MRI/CT	Efficient high-res output	Complex pipeline
30	Zhang et al. (2023)	Bayesian DL	Uncertainty-aware NN	Medical imaging	Provides confidence maps	Computational overhead

Analysis of Literature Review

The comparative analysis of the 30 studies on inverse modelling techniques for medical image reconstruction demonstrates a clear and structured evolution from classical mathematical inversion methods to advanced deep learning and physics-informed generative frameworks. Early approaches (Studies 1–10) primarily relied on deterministic reconstruction principles such as filtered back-projection, Tikhonov regularization, and iterative optimization techniques. These methods treated image reconstruction as a well-defined inverse problem governed by explicit mathematical operators. While highly interpretable and theoretically grounded, they were limited by sensitivity to noise, incomplete sampling, and rigid assumptions such as smoothness or sparsity, which restricted their performance in complex clinical imaging scenarios.

In contrast, the second phase (Studies 11–20) marks a transition toward data-driven inverse modelling, where deep learning architectures such as convolutional neural networks, variational networks, GANs, and unrolled optimization models replace explicit inversion formulas. These methods learn the inverse mapping directly from data, enabling significantly improved reconstruction speed and better suppression of noise and artifacts. Hybrid models, such as variational networks and learned primal-dual frameworks, attempt to combine physical imaging constraints with deep learning flexibility, offering improved stability and interpretability compared to purely data-driven approaches. However, these models still depend heavily on large annotated datasets and often suffer from limited generalization across different imaging devices and clinical environments.

The most recent phase (Studies 21–30) introduces advanced generative and physics-integrated architectures, including diffusion models, score-based generative networks, transformers, graph neural networks, and physics-informed neural networks. These models redefine inverse reconstruction as a probabilistic inference process rather than deterministic inversion. Diffusion and score-based models, in particular, provide highly realistic reconstructions even under extreme under sampling conditions, while transformer-based architectures improve global feature consistency through self-attention mechanisms. Physics-informed models enhance reliability by embedding imaging constraints directly into the learning process, and Bayesian frameworks introduce uncertainty quantification, which is critical for clinical decision-making. Despite their superior reconstruction quality and robustness, these approaches are computationally intensive and face challenges in real-time clinical deployment.

Overall, the comparative analysis highlights a fundamental shift in the field from classical analytical inversion to deep learning-based approximation and finally to hybrid physics–AI generative systems. Classical methods offer interpretability but limited adaptability, deep learning models provide speed and accuracy but reduced generalization, and modern generative models achieve state-of-the-art reconstruction quality but at high computational cost. The emerging consensus across these studies is that future research will increasingly focus on hybrid frameworks that integrate physical modelling, data-driven learning, and uncertainty quantification to achieve robust, efficient, and clinically reliable medical image reconstruction systems.

Discussion

The advancements in inverse modelling techniques for medical image reconstruction have profound implications for both clinical practice and software engineering. From a practical standpoint, improved reconstruction algorithms enable higher-quality imaging with reduced radiation exposure and faster acquisition times, directly benefiting patient safety and diagnostic accuracy. The integration of deep learning models into reconstruction pipelines has transformed traditional imaging systems into intelligent platforms capable of adaptive and context-aware processing. In the context of software engineering, the deployment of inverse modelling algorithms necessitates robust system design, scalability, and integration with existing healthcare infrastructure. Modern reconstruction systems must support high-throughput data processing, real-time inference, and interoperability with standards such as DICOM. The incorporation of AI models introduces additional requirements for version control, continuous integration, and automated testing, aligning with DevOps and DevSecOps practices. Ensuring the reliability and security of these systems is critical, particularly in safety-critical medical environments.

The role of AI-assisted reconstruction extends beyond image enhancement to include decision support, anomaly detection, and predictive analytics. Generative models, such as diffusion networks, offer capabilities for uncertainty quantification and probabilistic inference, which are essential for clinical trust. However, these models also introduce risks, including hallucinated features and lack of interpretability, which can compromise diagnostic reliability. Addressing these challenges requires the development of explainable AI frameworks and rigorous validation protocols. Another significant consideration is the ethical and privacy implications of AI-driven reconstruction. Techniques such as federated learning provide promising solutions for collaborative model development without compromising patient data privacy. However, they introduce new challenges related to communication efficiency, model synchronization, and security vulnerabilities. Ensuring compliance with regulatory standards and maintaining data integrity are essential for widespread adoption.

Future research directions are likely to focus on the development of unified frameworks that combine physics-based modelling, deep learning, and probabilistic inference. The integration of transformers and attention mechanisms offers opportunities for capturing complex spatial dependencies, while advances in hardware acceleration may address computational limitations. Additionally, the adoption of self-supervised and unsupervised learning techniques can reduce dependency on labeled datasets, enabling broader applicability across diverse imaging modalities. Despite significant progress, several open challenges remain. These include improving model generalization across different imaging devices, enhancing interpretability, reducing computational complexity, and establishing standardized evaluation benchmarks. Addressing these issues will require interdisciplinary collaboration between researchers in medical imaging, machine learning, and software engineering.

Conclusion

This systematic review provides a comprehensive analysis of inverse modelling techniques for medical image reconstruction, covering developments from 2018 to 2025. The study highlights the evolution of reconstruction methods from classical optimization-based approaches to advanced hybrid frameworks that integrate deep learning and physics-based modelling. The findings demonstrate that while deep learning has significantly improved reconstruction quality and efficiency, it also introduces challenges related to generalization, interpretability, and computational cost. One of the key contributions of this review is the identification of emerging trends in inverse modelling, including the adoption of generative models, physics-informed neural networks, and self-supervised learning techniques. These approaches address critical limitations of traditional methods, enabling more robust and data-efficient reconstruction. The review also emphasizes the importance of probabilistic modelling and uncertainty quantification, which are essential for clinical reliability and decision-making. From a software engineering perspective, the integration of inverse modelling techniques into medical imaging systems requires careful consideration of scalability, security, and interoperability. The adoption of DevOps and DevSecOps practices is essential for ensuring the reliability and maintainability of AI-driven reconstruction systems. Furthermore, the incorporation of privacy-preserving techniques such as federated learning highlights the growing importance of ethical considerations in AI development. The analysis reveals several research gaps that warrant further investigation. These include the need for standardized evaluation frameworks, improved model interpretability, and enhanced generalization across diverse imaging conditions. Additionally, reducing the computational complexity of advanced models, particularly generative and diffusion-based approaches, remains a critical challenge for real-time clinical applications. Looking forward, the future of inverse modelling in medical image reconstruction lies in the development of unified, hybrid frameworks that seamlessly integrate physics-based principles with advanced AI techniques. Such frameworks have the potential to revolutionize medical imaging by enabling faster, more accurate, and more reliable reconstruction processes. The continued advancement of this field will depend on interdisciplinary collaboration, technological innovation, and the establishment of robust evaluation standards. In conclusion, inverse modelling techniques represent a cornerstone of modern medical imaging, with significant implications for healthcare delivery and software engineering. This review provides a structured foundation for understanding current methodologies and identifying future research directions, contributing to the ongoing advancement of intelligent medical imaging systems.

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