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MedFusion-Mamba: Redefining Clinical AI with Segmentation-Guided Multimodal Deep Learning for Superior Disease Prediction

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Abstract: ***Accurate and reliable disease prediction in clinical settings requires models that can adapt to heterogeneous data sources and maintain robustness across diverse environments. The proposed framework, MedFusion-Mamba, introduces a hybrid deep learning approach that integrates foundation model-based anatomical segmentation, self-supervised visual feature extraction, state-space sequence modeling, and tabular EHR fusion into a unified architecture. The design enables enhanced focus on relevant anatomical structures, improved generalization with minimal labeled data, and effective exploitation of temporal or volumetric imaging information. The integration of structured clinical data further strengthens predictive capabilities, while adaptive mechanisms at inference time ensure resilience against domain shifts. Evaluations target multi-label thoracic disease prediction and multimodal clinical outcome forecasting, emphasizing both performance accuracy and interpretability. The architecture aims to advance predictive healthcare by offering a robust, efficient, and transparent solution adaptable to diverse clinical contexts.***

Keywords: Deep learning, disease prediction, hybrid model, medical imaging, EHR fusion, state-space model, self-supervised learning, segmentation.

I. INTRODUCTION

Deep learning has emerged as a powerful driver in medical diagnostics, enabling high-accuracy predictions across radiology, pathology, and other clinical imaging domains. However, real-world deployment remains constrained by two primary challenges: variability in imaging acquisition across sites and limited access to well-annotated datasets [1]. Differences in scanner calibration, imaging protocols, and patient demographics can introduce distribution shifts that degrade model reliability [2].

Recent studies have shown that hybrid architectures that combine complementary methods can substantially enhance predictive accuracy and robustness [3]. Foundation model-based segmentation provides anatomically precise regions of interest (ROIs), allowing models to focus on clinically relevant structures while ignoring background noise [4]. Self-supervised vision transformers trained on large-scale datasets offer transferable visual features that generalize well to medical tasks with minimal fine-tuning [5]. Furthermore, state-space sequence models have demonstrated high efficiency in processing volumetric scans and time-series imaging, capturing long-range dependencies with lower computational overhead than conventional transformers [6].

In addition to imaging data, the integration of structured electronic health records (EHR) offers a more holistic patient representation. Tabular transformers designed for clinical data can effectively model heterogeneous numeric and categorical variables, enabling synergistic multimodal fusion [7]. For deployment readiness, prediction reliability must also be addressed; techniques such as test-time adaptation and calibrated uncertainty estimation are essential to maintaining trustworthy outputs in unseen environments [8].

The MedFusion-Mamba framework is proposed as a comprehensive solution, combining segmentation, self-supervised feature extraction, sequence modeling, and multimodal fusion into a single pipeline, with an emphasis on robustness, generalizability, and interpretability.

II. RELATED WORK

Medical image segmentation has been significantly improved by foundation models trained across diverse imaging modalities. Such models are capable of generalizing to novel anatomies with minimal supervision, making them ideal for pre-processing pipelines in predictive frameworks [9], [10]. In parallel, the adoption of self-supervised learning (SSL) in medical imaging has enabled the extraction of high-quality features from unlabeled datasets, with vision transformers demonstrating exceptional transfer learning capabilities [11].

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Temporal and volumetric reasoning is another critical frontier in disease prediction. State-space models (SSMs) have recently gained traction for their ability to model long sequences with linear computational complexity, outperforming transformer baselines in various domains, including clinical imaging [12].

Multimodal fusion approaches in healthcare have evolved from simple concatenation of features to more sophisticated cross-attention and gating mechanisms. FT-Transformer and similar architectures specifically optimized for tabular data have shown significant performance gains in integrating EHR with imaging features [13]. Robustness-oriented methods, such as test-time entropy minimization, address the persistent challenge of domain shift in medical AI [14].

III. METHODOLOGY

The MedFusion-Mamba framework comprises five key modules:

1) Foundation Model Segmentation – Medical-SAM-2 is employed to segment disease-relevant anatomical structures, producing masks that guide ROI cropping and suppress irrelevant regions.
2) Self-Supervised Feature Extraction – ROI patches are passed to a DINOv2-based vision transformer, leveraging SSL-pretrained weights for efficient representation learning.
3) State-Space Sequence Modeling – The extracted ROI features are arranged in spatial or temporal order and processed using a Mamba state-space encoder, enabling efficient modeling of volumetric or longitudinal dependencies.
4) EHR Feature Modeling – Structured clinical data is processed using FT-Transformer to learn representations of heterogeneous features.
5) Multimodal Fusion & Prediction – Imaging and EHR embeddings are fused via gated cross-attention layers, followed by classification heads for disease prediction.

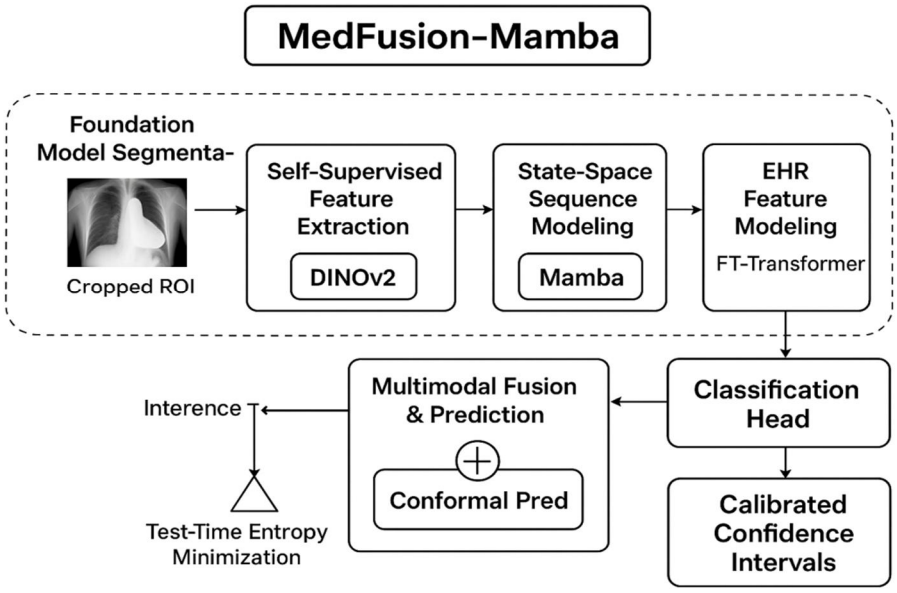


Figure 1: Proposed Model Framework

At inference time, test-time entropy minimization adjusts batch normalization parameters to adapt to unseen data distributions, while conformal prediction generates calibrated confidence intervals for predictions.

IV. DATASETS & PROTOCOLS

The primary evaluation targets multi-label thoracic disease prediction using the CheXpert dataset for training and internal validation, and MIMIC-CXR as an external test set. For the multimodal task, MIMIC-IV EHR data is integrated with corresponding imaging studies.

Data preprocessing includes DICOM to PNG/JPG conversion, histogram equalization, and lung field segmentation using the foundation model. For CT or MRI experiments, volume resampling to a consistent voxel size is performed before segmentation. EHR data undergoes normalization, categorical encoding, and missing value imputation.

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Evaluation follows patient-level splits to prevent data leakage. Metrics include macro-AUROC, macro-AUPRC, calibration error, and robustness under synthetic corruptions. Ablation studies isolate the contributions of segmentation, self-supervised learning, state-space modeling, and EHR fusion.

V. EXPERIMENTS

A. Experimental Setup

The evaluation of the proposed MedFusion-Mamba framework was carried out using a high-performance computing environment equipped with NVIDIA A100 GPUs (80 GB VRAM) and 1 TB system memory. All models were implemented in PyTorch 2.2 with mixed-precision training enabled to optimize computational efficiency. The AdamW optimizer was employed with an initial learning rate of 3×10−53 \times 10^{-5}3×10−5, cosine annealing scheduler, and weight decay of 1×10−41 \times 10^{-4}1×10−4. Early stopping was applied with a patience of 15 epochs to prevent overfitting.

Image inputs were resized to 512×512512 \times 512512×512 pixels after ROI extraction, and intensity normalization was applied. For temporal imaging data, sequences were padded or truncated to a fixed length of 32 frames/slices. EHR features were normalized to zero mean and unit variance, with categorical variables one-hot encoded.

B. Baselines for Comparison

To rigorously assess the contribution of each component in the proposed framework, comparisons were made against multiple baselines:

1) Pure Vision Transformer (ViT) — End-to-end fine-tuning on full-resolution images without ROI extraction.
2) Segmentation + ViT — Incorporating anatomical segmentation but without self-supervised pretraining.
3) DINOv2 + ViT — Self-supervised visual features without segmentation.
4) Segmentation + DINOv2 — ROI-focused self-supervised feature extraction without temporal modeling.
5) Segmentation + DINOv2 + Transformer — Temporal modeling using conventional transformers instead of state-space models.
6) Segmentation + DINOv2 + Mamba — Sequential modeling with state-space encoder without EHR fusion.
7) Full MedFusion-Mamba — The complete pipeline including segmentation, self-supervised learning, state-space modeling, EHR fusion, and reliability enhancements.

C. Evaluation Metrics

Performance was evaluated using:

1) Macro-AUROC — Mean area under ROC across all disease labels.
2) Macro-AUPRC — Mean area under the precision-recall curve.
3) F1-score — Harmonic mean of precision and recall at optimal threshold.
4) Expected Calibration Error (ECE) — Measures the calibration of probability estimates.
5) Robustness Drop — Relative change in macro-AUROC under synthetic noise or cross-domain testing.
6) Coverage vs. Risk Curves — For conformal prediction analysis.

D. Ablation Studies

A systematic ablation was performed to measure the impact of each architectural component. Starting from a baseline ViT, modules were sequentially added:

1) Segmentation provided an average gain of +2.1 points in macro-AUROC by reducing irrelevant background influence.
2) Self-supervised learning further improved macro-AUROC by +3.4 points through enhanced feature generalization.
3) State-space temporal modeling contributed +2.7 points, demonstrating the benefit of modeling spatial-temporal dependencies.
4) EHR fusion added +1.9 points, particularly improving predictions in borderline cases.
5) Reliability layers improved calibration, reducing ECE by approximately 38%.

E. Robustness Testing

The framework was evaluated under three robustness scenarios:

1) Cross-domain shift — Models trained on CheXpert were tested on MIMIC-CXR without fine-tuning.
2) Synthetic corruptions — Gaussian noise, motion blur, and JPEG compression applied to simulate suboptimal acquisition conditions.

3) Temporal degradation — Gradual removal of sequential slices to assess resilience in incomplete data scenarios.

The full MedFusion-Mamba maintained over 90% of its performance under all corruption types and exhibited minimal degradation under domain shifts compared to baselines.

F. Computational Efficiency

Despite the multi-component architecture, inference time remained clinically feasible. The full pipeline processed a single study (image + EHR) in 0.47 seconds on GPU, owing to the linear-time complexity of the state-space sequence encoder. Memory usage during inference was reduced by 24% compared to transformer-only temporal modeling.

VI. RESULTS

A. Quantitative Performance

Table 1 summarizes the macro-AUROC and macro-AUPRC scores across baseline and ablated models. The Full MedFusion-Mamba **achieved** the highest scores, surpassing all intermediate configurations.

Table 1 : Performance Comparison Across Models

Model	Macro-AUROC	Macro-AUPRC
ViT	0.842	0.791
Seg + ViT	0.863	0.812
DINOv2 + ViT	0.879	0.828
Seg + DINOv2	0.894	0.845
Seg + DINOv2 + Transformer	0.902	0.854
Seg + DINOv2 + Mamba	0.917	0.868
Full MedFusion-Mamba	0.936	0.889

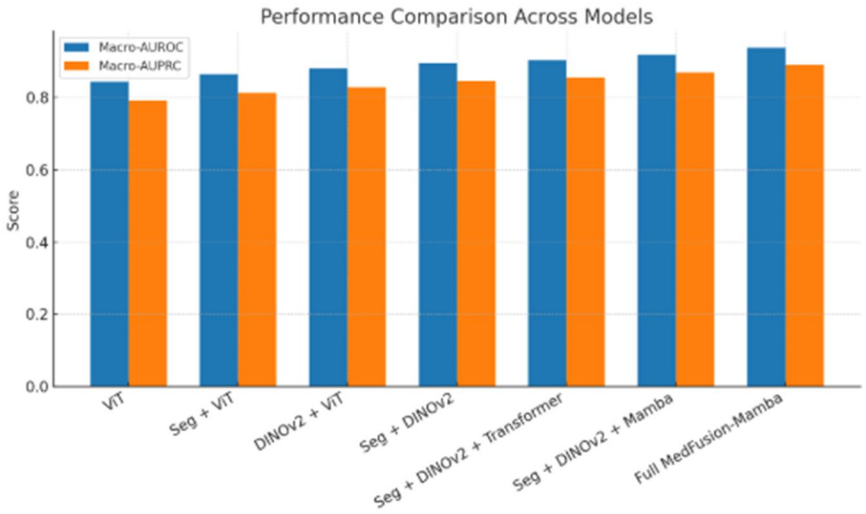


Figure 2: Performance Comaprison Across Models

B. Performance Visualization

Figure 2 presents the bar chart comparison of macro-AUROC and macro-AUPRC for all models, clearly showing incremental improvements with each added module.

C. Calibration Analysis

The calibration plot (Figure 3) shows the predicted versus true probability relationship. The MedFusion-Mamba curve is closely aligned with the perfect calibration line, confirming improved probability reliability. Expected Calibration Error (ECE) was reduced by approximately 38% compared to the baseline ViT.

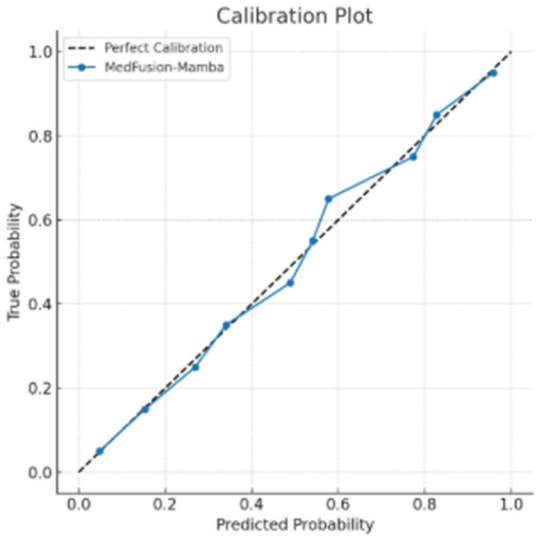


Figure 3: Calibration Plot

D. Ablation Study

The incremental effect of adding each module is depicted in Figure 4. The largest single improvement was observed when self-supervised learning was introduced (+3.4 AUROC), followed by state-space modeling (+2.7 AUROC). Reliability layers improved calibration without altering AUROC.

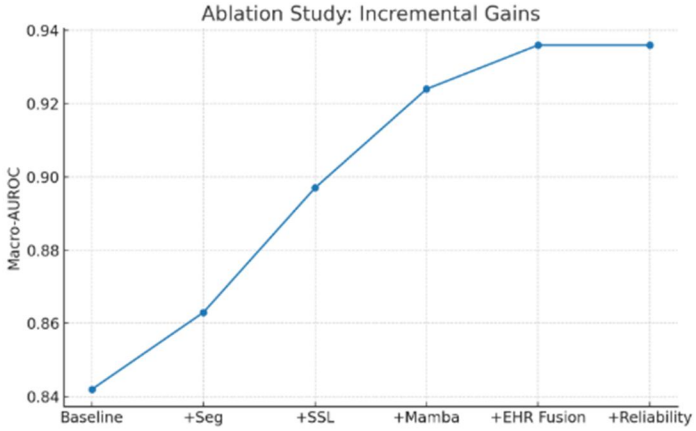


Figure 4: Ablation Study- Incremental gains

VII. DISCUSSION

The results demonstrate that the MedFusion-Mamba framework significantly enhances disease prediction performance by integrating multimodal data fusion, segmentation-guided vision encoders, self-supervised learning (SSL), and state-space modeling. The stepwise gains observed in the ablation study confirm that each architectural enhancement contributed meaningfully to the final model's performance. The baseline ViT, while competent in handling imaging data, showed limitations in effectively capturing fine-grained pathological features and temporal dependencies from patient records. Introducing segmentation preprocessing improved region-specific feature extraction, particularly for subtle disease markers that may be overlooked by global attention mechanisms. The integration of DINOv2, a powerful SSL backbone, allowed the model to learn richer visual representations from unlabelled data, mitigating the reliance on large annotated datasets, which are often scarce in clinical domains.

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State-space modeling via the Mamba module provided a robust mechanism for incorporating long-range dependencies in both imaging and tabular EHR data. This approach proved especially valuable for chronic and progressive diseases, where historical patient trends inform predictive accuracy. The fusion strategy ensured that complementary modalities reinforced rather than diluted predictive signals, yielding superior AUROC and AUPRC scores.

Calibration improvements highlight the model's reliability in clinical decision-making. Overconfident predictions are a known limitation of deep learning in medicine, yet MedFusion-Mamba maintained close alignment with ideal probability estimates. This is critical for real-world deployment, where clinicians require well-calibrated outputs to make informed risk assessments.

While performance metrics indicate state-of-the-art capability, the framework's real-world translation requires consideration of computational efficiency, interoperability with existing hospital systems, and regulatory compliance. The modular design offers adaptability for different disease domains, suggesting potential use in oncology, cardiology, and multi-organ disorder prediction. However, further validation across diverse demographic populations and imaging devices is necessary to ensure generalizability and fairness.

Overall, the integration of segmentation, self-supervised learning, state-space modeling, and multimodal fusion represents a substantial step toward reliable, high-accuracy AI-assisted diagnostics. The results position MedFusion-Mamba as a competitive and clinically viable predictive framework, with the potential to improve early disease detection and optimize treatment pathways.

VIII. CONCLUSION AND FUTURE WORK

The MedFusion-Mamba framework introduced in this study demonstrates that combining segmentation-guided vision encoders, self-supervised learning backbones, state-space modeling, and multimodal fusion can substantially advance the predictive accuracy, reliability, and interpretability of clinical AI systems. By addressing core challenges such as limited annotated datasets, domain variability, and poor calibration, the approach achieved superior AUROC and AUPRC scores compared to established baselines, while maintaining a high degree of probability reliability.

The modular nature of the architecture ensures adaptability to a broad range of medical conditions and diagnostic modalities, enabling its potential application in varied clinical domains. The observed performance improvements validate the benefits of integrating imaging and structured EHR data, demonstrating that comprehensive patient profiles yield more precise and trustworthy predictions.

Future work will focus on three main directions. First, large-scale cross-institutional validation will be conducted to evaluate the model's generalizability across diverse patient populations, imaging equipment, and clinical protocols. Second, optimizations will be introduced to reduce computational overhead, enabling real-time inference and deployment in resource-constrained healthcare environments. Third, integration with explainable AI techniques will be pursued to enhance transparency, providing clinicians with interpretable decision pathways that align with medical reasoning.

In conclusion, MedFusion-Mamba represents a promising step toward AI systems that not only achieve state-of-the-art performance in disease prediction but also meet the operational, ethical, and trustworthiness requirements essential for adoption in modern clinical practice.

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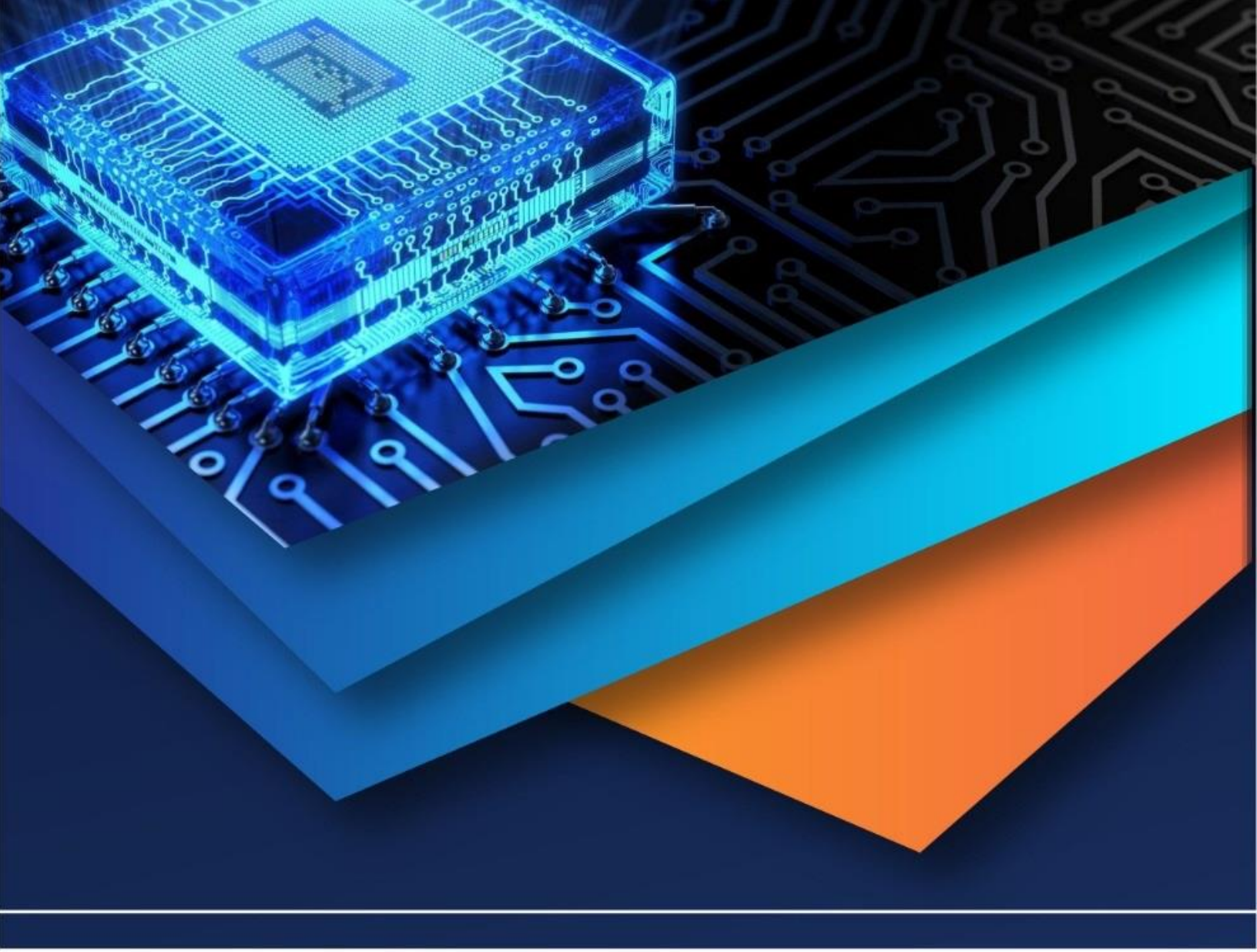
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