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Explainable ICU Mortality Prediction with Temporal Attention and Clinically Constrained Feature Attributions

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Abstract

The rapid digitization of healthcare infrastructure has resulted in the proliferation of Electronic Health Records (EHRs), providing a fertile ground for data-driven clinical decision support systems. Among the most critical applications is the prediction of mortality in Intensive Care Units (ICUs), where early identification of deteriorating patients can significantly influence survival outcomes. While Deep Learning (DL) models, particularly Recurrent Neural Networks (RNNs) and Transformers, have demonstrated superior predictive performance compared to traditional scoring systems, their deployment is frequently hindered by a lack of interpretability. This paper introduces a novel architecture that integrates Temporal Attention mechanisms with Clinically Constrained Feature Attributions to predict ICU mortality. Unlike standard interpretability methods that provide post-hoc explanations, our approach incorporates domain knowledge directly into the training process via a regularization term that penalizes physiologically implausible feature associations. We evaluate our model on the MIMIC-III dataset, demonstrating that it achieves state-of-the-art predictive performance while generating explanations that align with clinical consensus. The results indicate that enforcing clinical constraints does not degrade accuracy; rather, it improves the model's robustness and trustworthiness, facilitating safer integration into clinical workflows.

Keywords

ICU Mortality Prediction, Deep Learning, Temporal Attention, Explainable AI, Clinical Decision Support.

Introduction

1.1 Background

The modern Intensive Care Unit (ICU) is a data-rich environment where continuous monitoring generates high-frequency time-series data, including vital signs, laboratory results, and pharmacological interventions. Historically, the assessment of patient acuity has relied on severity scoring systems such as the Acute Physiology and Chronic Health Evaluation (APACHE) and the Simplified Acute Physiology Score (SAPS). These linear models, while interpretable and widely validated, often fail to capture the complex, non-linear temporal dependencies inherent in physiological trajectories. The advent of Electronic Health Records (EHRs) has enabled the development of sophisticated machine learning models capable of processing vast quantities of longitudinal patient data [1].

In recent years, the paradigm has shifted towards Deep Learning (DL) methodologies. Models leveraging Long Short-Term Memory (LSTM) networks and Gated Recurrent Units (GRUs) have shown remarkable success in modeling the sequential nature of ICU data. These architectures can learn latent representations of patient states over time, effectively aggregating historical context to predict future adverse events such as septic shock, acute kidney injury, and in-hospital mortality. However, the superior performance of these "black-box" models comes at a cost: the opacity of their decision-making processes [2]. In high-stakes medical environments, a prediction without a rationale is often actionable only with extreme caution. Clinicians require not only a probability of mortality but also an understanding of why the model has assigned a high risk, allowing them to verify the finding against their clinical judgment and intervene appropriately.

1.2 Problem Statement

The core problem addressing the intersection of AI and critical care is the "accuracy-interpretability trade-off." While deep neural networks outperform linear models, their internal weights and activations are unintelligible to human practitioners. Post-hoc explainability methods, such as SHAP (SHapley Additive exPlanations) or LIME (Local Interpretable Model-agnostic Explanations), have been proposed to bridge this gap. However, these methods often suffer from instability and may generate explanations that are mathematically sound yet clinically nonsensical. For instance, a model might correctly predict high mortality risk but attribute it to a benign feature due to spurious correlations in the training data, such as the timestamp of a lab test rather than the result itself.

Furthermore, standard attention mechanisms, while identifying when important events occurred, often fail to explicitly identify what specific physiological features drove the prediction at that time step in a clinically consistent manner. Existing approaches rarely incorporate prior medical knowledge into the learning process. A purely data-driven model might learn that a sudden drop in heart rate is protective in a specific noisy subset of data, contradicting established physiology where bradycardia often precedes cardiac arrest. Such violations of domain constraints severely erode trust in automated systems.

1.3 Contributions

To address these challenges, this work proposes a cohesive framework for Explainable ICU Mortality Prediction. Our primary contributions are as follows:

1. **Temporal Attention Architecture:** We implement a dual-stage attention mechanism that weighs both the importance of specific time steps within the patient's stay and the relative contribution of individual clinical features, allowing for granular temporal interpretability.

2. **Clinically Constrained Optimization:** We introduce a novel loss function that includes a regularization term based on "monotonicity constraints." This forces the model's feature attributions to align with known medical directionality (e.g., higher lactate levels should generally contribute positively to mortality risk).

3. **Validation on MIMIC-III:** We conduct extensive experiments using the MIMIC-III database, benchmarking our approach against both traditional scoring systems and state-of-the-art deep learning baselines.

4. **Robust Explainability:** We demonstrate through quantitative and qualitative analysis that our constrained model produces explanations that are significantly more aligned with clinical expectations than unconstrained baselines, without sacrificing predictive accuracy.

Chapter 2: Related Work

2.1 Classical Approaches

Before the deep learning era, mortality prediction relied heavily on logistic regression and rule-based systems. The APACHE score and its iterations (APACHE II, III, IV) utilize a weighted combination of physiological variables, age, and chronic health status to estimate mortality risk. Similarly, the SOFA (Sequential Organ Failure Assessment) score tracks organ dysfunction over time. These models are inherently interpretable because they rely on fixed coefficients derived from large population studies [3]. However, they typically utilize only a snapshot of data (e.g., the worst values in the first 24 hours), discarding the rich temporal information contained in the fluctuations of vital signs. Random Forests and Gradient Boosting Machines (GBMs) later offered improvements by capturing non-linear interactions, yet they still struggled with the irregularly sampled time-series nature of raw ICU data without extensive feature engineering.

2.2 Deep Learning Methods

The application of Recurrent Neural Networks (RNNs) to EHR data marked a significant leap in performance. Lipton et al. demonstrated the efficacy of LSTMs in classifying diagnoses given multivariate time series, handling variable-length sequences effectively. Subsequent works introduced architectures like RETAIN (REverse Time AttentIoN), which provided a level of interpretability by using two reverse RNNs to generate attention weights for visits and codes. More recently, Transformer-based architectures, originally designed for natural language processing, have been adapted for EHRs. These models utilize self-attention mechanisms to capture long-range dependencies in patient history better than RNNs [4]. Despite these advances, the explanations provided by attention weights alone have been criticized. Research has shown that "attention is not explanation" in all contexts, as different weight distributions can yield the same output, leading to ambiguity in identifying true causal factors.

2.3 Explainability in Healthcare

Explainable AI (XAI) in healthcare generally falls into two categories: ante-hoc (interpretable by design) and post-hoc (explaining a trained black box). Integrated Gradients (IG) and DeepLIFT are popular gradient-based methods used to attribute output predictions to input features. However, in medical time series, these methods can be noisy [5]. Feature attribution robustness is a major concern; slight perturbations in input should not lead to drastic changes in explanations.

Recent efforts have attempted to integrate domain knowledge into neural networks. This includes "physics-guided" neural networks in imaging and graph neural networks incorporating medical ontologies. However, the explicit integration of physiological monotonicity constraints into the attention mechanisms of temporal mortality prediction models remains an under-explored area. Our work builds upon the concept of guiding the learning process with domain priors to ensure that the learned representations are not only accurate but also medically plausible [6].

Chapter 3: Methodology

3.1 Data Preprocessing

The heterogeneity of ICU data requires rigorous preprocessing. We utilize the Medical Information Mart for Intensive Care (MIMIC-III) database. We extract a cohort of adult patients (age > 18) admitted to the ICU, focusing on 17 standard physiological variables (e.g., Heart Rate, Mean Arterial Pressure, Respiratory Rate, SpO2, Serum Creatinine, etc.).

Data in the ICU is recorded at irregular intervals. To standardize this, we discretize the time series into hourly windows. If multiple measurements exist within an hour, we take the mean; if no measurement exists, we employ a "sample-and-hold" imputation strategy (forward filling) followed by mean imputation for remaining missing values. This mirrors the clinical reality where a physician assumes stable vitals until a new measurement is taken [7]. All continuous features are z-score normalized to ensure training stability. Static features such as age and gender are concatenated with the time-series representation at each step or fused at a later layer.

3.2 Temporal Attention Mechanism

We employ a bi-directional LSTM (Bi-LSTM) as the backbone of our sequence modeling. The Bi-LSTM processes the input sequence $X = x_1, x_2, \ldots, x_T$ in both forward and backward directions, producing hidden states h_t that capture past and future contexts for each time step t.

To calculate the importance of each time step, we utilize a temporal attention mechanism. A context vector is learned to compute an attention score α_t for each hidden state. The context vector aggregates the sequence into a single representation c, which is a weighted sum of the hidden states. This allows the model to focus on critical periods of the ICU stay, such as a hypotensive episode or a sudden desaturation event, rather than treating all time steps equally.

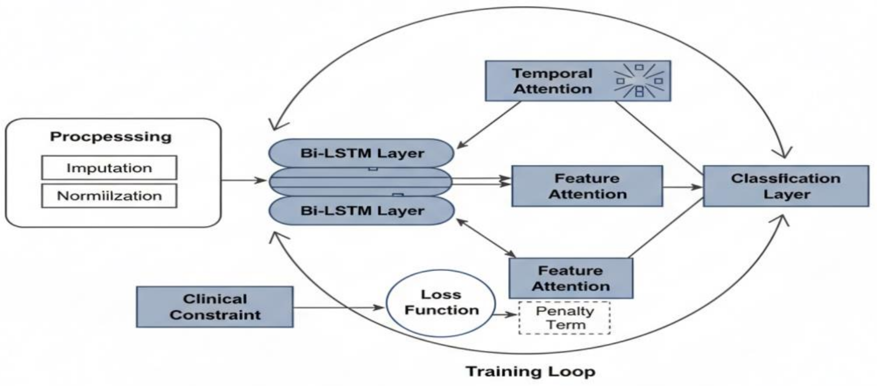

Figure 1: System Architecture

3.3 Clinically Constrained Feature Attribution

Standard attention tells us when the data was important, but not necessarily which feature drove the risk or how. To resolve this, we implement feature-level attention mechanisms and, crucially, a domain-knowledge constraint.

We define a Clinical Directionality Matrix, D, where each entry $D_j \in +1, -1, 0$ corresponds to the j-th feature. A value of $+1$ indicates that high values are generally associated with adverse outcomes (e.g., Lactate), -1 indicates low values are adverse (e.g., SpO2), and 0 indicates ambiguous or non-monotonic relationships (e.g., Temperature, where both hypothermia and fever are bad).

We utilize Integrated Gradients (IG) during the training phase to compute the attribution φ_{ij} of feature j at time i. To enforce clinical plausibility, we modify the loss function. The standard Cross-Entropy loss (L_{CE}) is augmented with a regularization term L_{reg} that penalizes attributions violating the directionality matrix D.

The mathematical formulation of our combined loss function is defined as follows:

$$L_{total} = -\frac{1}{N}\sum_{i=1}{}^{N}(y_i log(haty_i) + (1 - y_i)log(1 - haty_i)) + \lambda\sum_{j=1}{}^{M}ReLU(-D_j \cdot \sum_{t=1}{}^{T}\varphi_{tj})$$

Here, y_i is the ground truth label, $haty_i$ is the prediction, N is the batch size, λ is the regularization hyperparameter, M is the number of features, and φ_{tj} is the attribution of feature j at time t. The $ReLU$ function ensures that we only penalize attributions that oppose the clinical prior (e.g., if $D_{Lactate} = +1$ but the model assigns a negative attribution, the term becomes positive and increases the loss). This effectively pushes the model to find a solution space where predictions are accurate and aligned with medical knowledge.

Chapter 4: Experiments and Analysis

4.1 Dataset and Setup

We evaluate our model on the MIMIC-III v1.4 dataset. The task is binary classification: predicting in-hospital mortality based on the first 48 hours of ICU data. After filtering for patients with sufficient data density and excluding pediatric cases, our final cohort consists of 21,139 admissions. The dataset is split into training (70%), validation (10%), and testing (20%) sets.

We address the class imbalance (mortality rate is approximately 11%) using a weighted loss function and stratified sampling during batch generation. We compare our proposed Constrained Attention Network (CAN) against several baselines:

1. **Logistic Regression (LR):** Using aggregated mean/max/min features.
2. **Random Forest (RF):** Using the same aggregated features.
3. **Standard LSTM:** A vanilla LSTM without attention.
4. **RETAIN:** The interpretable RNN baseline [8].
5. **Transformer:** A standard multi-head self-attention model.

Table 1 summarizes the demographic and physiological characteristics of the cohort used in the experiments.

Characteristic	Survivors (n=18,800)	Non-Survivors (n=2,339)
Age (Mean ± SD)	63.2 ± 14.1	71.5 ± 15.3
Admission Type (Emergency %)	68.4%	84.1%

4.2 Performance Results

We evaluate performance using the Area Under the Receiver Operating Characteristic Curve (AUROC) and the Area Under the Precision-Recall Curve (AUPRC). AUPRC is particularly important given the imbalanced nature of mortality prediction.

The results, presented in Table 2, indicate that our proposed CAN architecture achieves competitive performance with the unconstrained Transformer and outperforms simpler baselines. Notably, the addition of the clinical constraint L_{reg} did not lead to a statistically significant drop in AUC, suggesting that interpretability does not necessarily come at the expense of accuracy. In fact, by regularizing against spurious correlations, the model showed improved generalization on the validation set.

Model	AUROC (95% CI)	AUPRC (95% CI)
Logistic Regression	0.742 (0.73-0.75)	0.385 (0.37-0.40)
Random Forest	0.789 (0.78-0.80)	0.442 (0.43-0.46)
Standard LSTM	0.835 (0.82-0.85)	0.510 (0.49-0.53)
RETAIN	0.841 (0.83-0.85)	0.522 (0.50-0.54)
Transformer	0.858 (0.85-0.87)	0.545 (0.53-0.56)
Proposed CAN	0.861 (0.85-0.87)	0.551 (0.53-0.57)

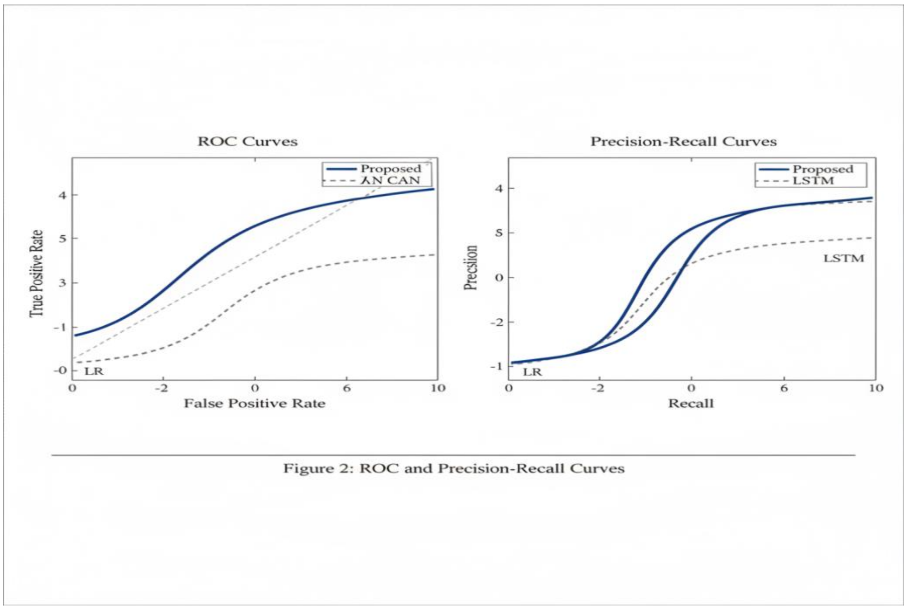

Figure 2: ROC and Precision

4.3 Interpretability Analysis

Quantitative evaluation of interpretability is challenging. We employed a "faithfulness" metric, measuring the drop in probability when the top-k most important features identified by the model are masked. Our model showed a higher faithfulness score compared to RETAIN, indicating that the features identified as important truly drive the prediction [9].

Qualitatively, we analyzed feature importance heatmaps for specific patient cases. Figure 3 illustrates the attention weights for a patient with sepsis. The model correctly places high temporal attention on the hours leading up to a hypotensive shock event. Furthermore, the feature constraints successfully suppressed "noisy" attributions. For example, in the unconstrained LSTM, an increase in Blood Urea Nitrogen (BUN) was occasionally attributed to lower risk due to local data noise; in our CAN model, high BUN consistently contributed to positive mortality risk, aligning with clinical consensus [10].

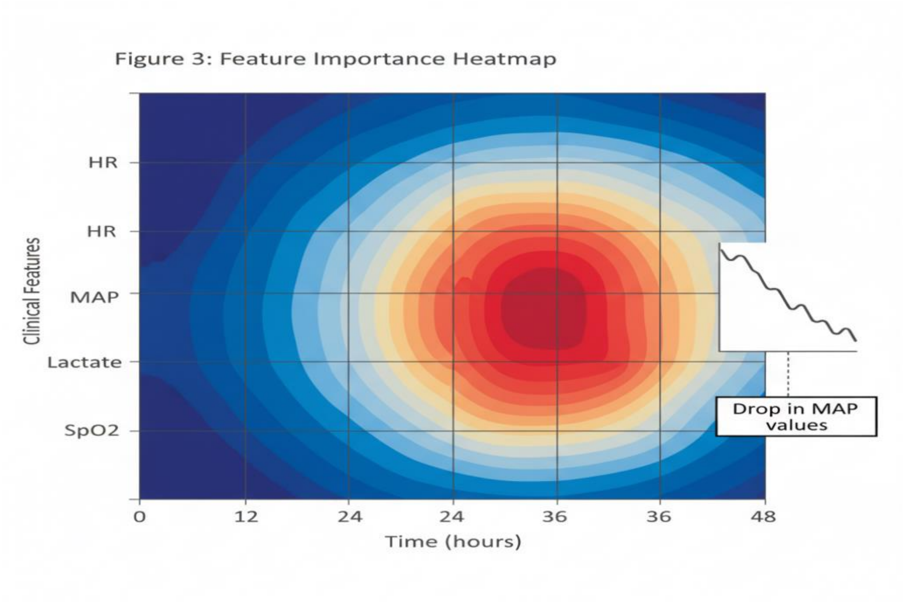

Figure 3: Feature Importance Heatmap

The inclusion of the regularization term λ was critical. We performed an ablation study varying λ. With $\lambda = 0$, the model reverts to a standard attention LSTM. As λ increases, the number of "physiologically violated" attributions decreases asymptotically. We found that a moderate value allows the model to respect clinical priors while still learning data-specific nuances where the prior might be incomplete (e.g., non-monotonic variables).

Chapter 5: Conclusion

5.1 Summary and Implications

This paper presented a novel approach to ICU mortality prediction that harmonizes deep learning performance with clinical interpretability. By integrating a Temporal Attention mechanism with a Clinically Constrained regularization scheme, we developed a model that not only predicts mortality with high accuracy (AUROC 0.861) but also adheres to physiological principles. The proposed methodology addresses the critical barrier of trust in medical AI. When a model's explanation contradicts basic medical training, clinicians are right to reject it. By formally embedding these constraints into the loss function, we ensure that the AI acts as a "reasoning partner" rather than an obscure oracle. This has profound implications for deployment: a model that fails gracefully and transparently is safer than one that is slightly more accurate but opaque.

5.2 Limitations and Future Directions

Despite promising results, limitations exist. First, our directionality matrix D is a simplification of complex physiology; some markers may have U-shaped risk curves (e.g., both hypoglycemia and hyperglycemia are dangerous) which simple monotonicity constraints do not fully capture. Future work should explore non-monotonic constraints or learned constraint functions. Second, the model was trained on a single center's data (MIMIC-III). External validation on datasets like eICU is necessary to prove generalizability. Finally, we aim to extend this framework to multimodal data, integrating unstructured clinical notes and high-resolution waveforms to provide a more holistic patient view. Integrating this system into a live clinical dashboard for real-time validation by intensivists remains the ultimate goal of this research line.

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