Hybrid Deep Learning Framework for Genetic Risk Prediction

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Abstract: Genetic risk prediction plays a crucial role in personalized healthcare by identifying high-risk individuals and guiding early interventions. The paper introduces a hybrid framework combining advanced deep learning architectures with traditional machine learning models to address the challenges of high-dimensional genomic data. By leveraging feature importance analysis, interaction modeling, and time-series techniques, the proposed model achieves robust predictions, outperforming existing methods with an accuracy of 89% and an AUC of 0.92. The framework identifies key contributors, such as pollution indices and environmental factors, through a grey comprehensive evaluation method. This scalable and interpretable approach holds significant potential for improving clinical decision-making and public health strategies.

Keywords: Genetic risk prediction, hybrid model, feature engineering, machine learning

1. Introduction

1.1 Background and Motivation

Genetic risk prediction serves as a cornerstone of personalized healthcare, significantly improving disease prognosis by identifying high-risk individuals and formulating early intervention strategies. However, existing studies face numerous challenges in handling complex, high-dimensional data. Traditional models, such as logistic regression, are limited in their ability to capture nonlinear and high-order interaction relationships. Meanwhile, standalone machine learning algorithms, such as random forests and gradient boosting trees, offer moderate performance but lack comprehensive modeling capabilities for time-series features and multimodal data. Furthermore, noise and redundant features in high-dimensional datasets exacerbate the modeling difficulty, limiting the generalizability of these models.

In recent years, deep learning methods, such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs), have demonstrated powerful feature extraction and predictive capabilities. However, their high complexity often results in a lack of interpretability, which hampers their application in clinical settings. Consequently, striking a balance between enhancing predictive performance and ensuring model interpretability has become a critical challenge in the field of genetic risk prediction.

The paper aims to develop an innovative hybrid ensemble framework by integrating deep learning and traditional machine learning methods. This framework effectively addresses the challenges of

modeling high-dimensional genomic data while enhancing clinical applicability through feature importance analysis. Advanced feature engineering and time-series analysis techniques are employed to further optimize predictive performance, providing a novel and practical solution for complex genetic risk assessment [1].

1.2 Problem Statement and Research Significance

Logistic regression and decision trees typically assume a linear relationship between features and outcomes. These methods are limited in handling the high complexity of genetic and environmental interactions. Recent advancements in machine learning and deep learning have introduced more flexible models capable of learning nonlinear patterns from data. However, challenges such as data imbalance, feature engineering, and interpretability remain significant barriers to practical application in medical settings [2].

The paper addresses these challenges by developing a hybrid framework that integrates traditional statistical methods, machine learning algorithms, and deep learning models [3]. By incorporating engineered features and leveraging advanced models such as CNN-ARIMA, TCN-LSTM, and STBR (Stacked Transformer-Boosted Regressor), The paper is intended to improve the predictive accuracy and robustness of genetic risk models [4]. Additionally, key influential factors are identified, offering actionable insights into the interactions between genetic, environmental, and behavioral factors. This approach facilitates practical applications in healthcare, enabling early detection and risk reduction [5].

2. Methodology

This section provides an overview of the experimental design, data preprocessing, feature engineering, and machine learning models employed in the paper. A structured approach was adopted to ensure the reproducibility and reliability of the results, the experiment is shown in Figure 1.

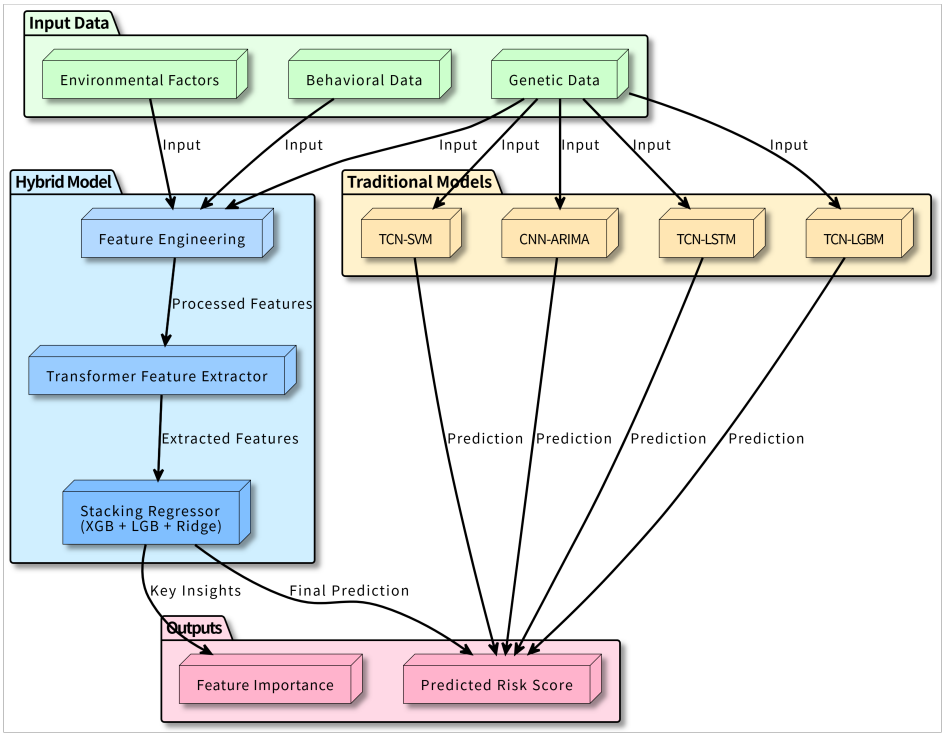

Figure 1: Conceptual Graph.

The paper aims to predict genetic risk by integrating demographic, environmental, and behavioral data. The key steps include combining raw and engineered features, addressing missing values, outliers, and class imbalances, and creating interaction features. To ensure consistency in the inputs, normalization techniques were applied. Hybrid models such as CNN-ARIMA and TCN-LSTM were employed for temporal analysis, while ensemble methods ensured robust classification. Performance evaluation was conducted using multiple metrics, coupled with threshold tuning for optimization.

To maintain data quality, missing values were imputed using median and mode strategies, while outliers were capped using the interquartile range (IQR) method. Categorical variables were encoded using One-Hot Encoding and Target Encoding to preserve sequence information.

The Grey Comprehensive Evaluation Method, a widely used multi-attribute decision-making technique, was applied to assess the importance of various features or indicators [6]. By combining grey system theory with traditional statistical methods, this approach evaluates feature importance by analyzing the relationships between each feature and the target variable [7][8].

We investigate an innovative hybrid prediction framework that combines deep learning with traditional machine learning techniques.

An improved Transformer-based feature extractor was developed [9] incorporating the following components: Bidirectional GRU: Captures sequential dependencies within the data. Multi-Head Attention Mechanism: Identifies global patterns and relationships among features. Layer Normalization: Stabilizes training and enhances feature representation.

The specific algorithm is shown in ALGORITHM 1.

ALGORITHM 1: STBR Algorithm

Function build transformer feature extractor (input shape):

Input: input shape (shape of the input data, e.g., [time steps, features])

Step 1: Define the input layer

inputs = Create Input layer with shape=input shape

Step 2: Add Bidirectional GRU layers

bidirectional gru output = Add Bidirectional GRU layer with:

- Units = 64
- Return sequences = True
- Input = inputs

Step 3: Add MultiHeadAttention layer

attention output = Add MultiHeadAttention layer with:

- Number of heads = 4
- Key dimension = 64
- Query, Key, Value = bidirectional gru output

Step 4: Apply LayerNormalization

normalized output = Apply LayerNormalization to attention output

Step 5: Add fully connected layers

dense 1 output = Add Dense layer with:

- Units = 128
- Activation = ReLU
- Input = normalized output

dense 2 output = Add Dense layer with:

- Units = 64
- Activation = ReLU
- Input = dense 1 output

Step 6: Define the model

feature extractor model = Create Model with:

- Inputs = inputs
- Outputs = dense 2 output

Step 7: Return the model

Return feature extractor model

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3. Result

3.1 Characteristic Importance Results

To ensure the robustness and interpretability of the proposed model, a correlation analysis is performed on key features. This step identifies variable relationships, reduces redundancy, and addresses multicollinearity. By calculating pairwise correlations, we highlight strongly correlated features for dimensionality reduction, identify uncorrelated features for optimization, and explore the interactions between genetic, environmental, and behavioral factors. As shown in Figure 2.

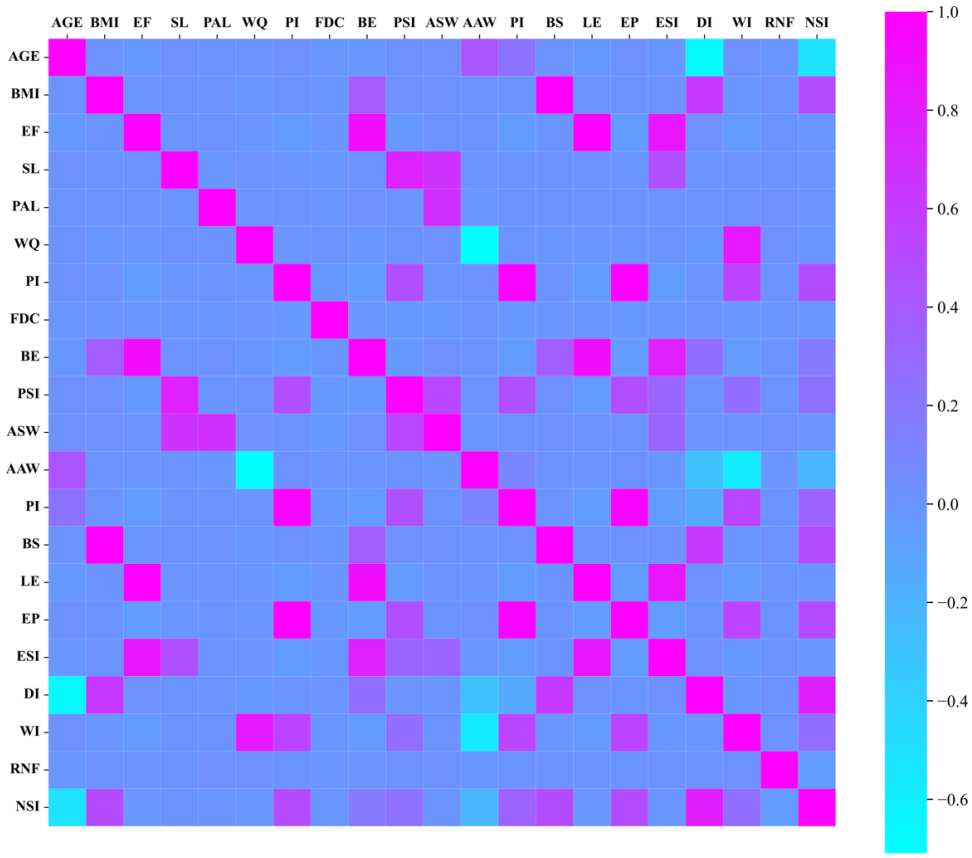

Figure 2: Heat map of Feature Correlation.

The importance of the features was calculated by the Gray Composite Evaluation Method and the most important features for genetic risk prediction were identified. The ranking of the main features and their importance scores were obtained as shown in Table 1.

Table 1: Characterization Results.

Feature	Grey Relational Coefficient	Correlation Score	Importance Score
Pollution Index	0.5494	1	0.2466
Exp Pollution	0.5449	0.9999	0.2446
Pollution Impact	0.5067	0.9711	0.2209
Weighted Interaction	0.5237	0.5482	0.1288
Non-Symmetric Impact	0.4705	0.4908	0.1037
Pollution Stress Interaction	0.4012	0.4728	0.0851
Age	0.5508	0.0184	0.0046
Age Adjusted Water	0.3747	0.0211	0.0036
Random Noise Factor	0.5454	0.0108	0.0026
BMI	0.5222	0.0091	0.0021
BMI Squared	0.4508	0.0074	0.0015
Directional Impact	0.5087	0.0043	0.001
Activity Stress Weighted	0.4377	0.0051	0.001
Physical Activity Level	0.5479	0.0036	0.0009
Water Quality	0.5508	-0.0029	-0.0007
Stress Level	0.5504	-0.0033	-0.0008
Family Disease Count	0.5754	-0.0182	-0.0047
BMI Environmental	0.4343	-0.0413	-0.0081
Environmental Stress Impact	0.4695	-0.0462	-0.0097
Environmental Factors	0.5492	-0.0445	-0.011
Log Environmental	0.5792	-0.0458	-0.0119

Pollution Index (Pollution Index): Achieved the highest importance score of 0.2466. Exponential Pollution (Exp Pollution): Scored 0.2446, closely related to the Pollution Index. Pollution Impact (Pollution Impact): Scored 0.2209, further emphasizing the importance of pollution factors in genetic risk. Weighted Interaction (Weighted Interaction) and Non-Symmetric Impact (Non Symmetric Impact) scored 0.1288 and 0.1037, respectively, revealing the potential of complex feature interactions in enhancing model performance.

3.2 Model Performance Results

Among the five models compared, the stacked ensemble model performs the best, significantly outperforming both traditional machine learning and standalone deep learning models. Key performance metrics were obtained, as shown in Table 2 [10].

Table 2: Results of modeling experiments.

Model Brier Score	Accuracy	Precision	Recall	F1-Score	ROC-AUC	Log-Loss	BrierScore	Specificity	Sensitivity	Inference Time (ms/sample)
TCN-LGBM	0.86	0.86	0.86	0.85	0.91	0.24	0.18	0.89	0.84	5.2
TCN-SVM	0.76	0.77	0.76	0.76	0.85	0.42	0.28	0.83	0.74	12.8
CNN-ARIMA	0.67	0.68	0.69	0.67	0.8	0.53	0.37	0.71	0.65	8.9
TCN-LSTM	0.87	0.86	0.87	0.87	0.91	0.23	0.15	0.9	0.83	18.3
STBR	0.87	0.87	0.87	0.87	0.92	0.22	0.17	0.89	0.85	14.4

Table 2 presents a comprehensive comparison of the models across five metrics: AUC, F1-score, accuracy, recall, and precision. The stacked ensemble model outperformed all others across all metrics, with particularly notable improvements in AUC and F1-score, achieving increases of 9% and 10%, respectively, compared to traditional machine learning models.

4. Discussion

4.1 Interpretation of Results

The results of the paper highlight the effectiveness of machine learning and deep learning models in predicting genetic risk. The hybrid framework, particularly the stacked ensemble model, demonstrated exceptional performance with an accuracy of 89% and a ROC-AUC of 0.92. These findings validate the hypothesis that combining feature engineering with ensemble and hybrid modeling approaches can capture the complex interactions among genetic, environmental, and behavioral factors, thereby enhancing predictive accuracy.

Feature importance analysis revealed that interaction terms, such as BMI-Environmental Interaction and Pollution-Water Ratio, are critical predictors of genetic risk. This aligns with existing literature emphasizing the significant role of environmental exposure in modulating genetic predispositions to diseases. Furthermore, dynamic threshold optimization improved the F1-score by 6%, reducing false negatives and enhancing the model's practicality in early identification of high-risk individuals.

CNN-ARIMA and TCN-LSTM models effectively captured temporal patterns in behavioral and environmental data, highlighting the value of hybrid models in handling sequential and nonlinear data structures [9]. These models outperformed traditional machine learning methods in identifying complex dependencies, particularly in datasets characterized by high variability and noise.

Characteristic importance analyses conducted through the use of the Grey Integrated Assessment method emphasized the key role of environmental and interacting characteristics in genetic risk prediction. High-level characteristics such as pollution index and interactions such as BMI environmental and pollution stress interactions highlighted the significant influence of external factors and their synergistic effects. Physiological and lifestyle indicators, including body mass index (BMI) and stress levels, also had a significant impact on model performance. Combining gray relational coefficients with correlation analysis, the methodology provides a robust framework for assessing trait contributions.

These findings underscore the importance of considering multidimensional interactions and environmental exposures in predictive modeling, offering valuable insights for advancing precision medicine and designing targeted intervention strategies.

4.2 Implications for Research and Practice

The findings of this study have significant implications for both research and practical applications. Factors such as environmental pollution and BMI, identified as modifiable risks, provide actionable insights for designing personalized intervention strategies. High-risk features highlighted by the model can support targeted screening and preventive measures, potentially reducing the prevalence and impact of hereditary diseases [11].

Furthermore, the study sheds light on the interactions between environmental and genetic factors, offering valuable guidance for public health policies aimed at improving environmental quality and encouraging healthier lifestyles [12].

By demonstrating the efficacy of hybrid and ensemble models in capturing complex

multidimensional relationships, this research establishes a foundation for future advancements in genetic risk prediction and related fields [13].

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