DEEP LEARNING ANALYSIS OF PLASMA CYTOKINE DATA FOR IMPROVED CORONARY ARTERY DISEASE IDENTIFICATION

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Abstract: Coronary Artery Disease (CAD) remains a leading cause of mortality worldwide, necessitating early and precise diagnostic strategies. Traditional detection methods are often invasive, costly, and limited in sensitivity, particularly during early-stage manifestation. In this study, we present an advanced, non-invasive framework for CAD detection using deep learning models trained on plasma cytokine profiles. Cytokines, as immune signaling molecules, reflect systemic inflammation and cardiovascular health, making them promising biomarkers for CAD. A comprehensive dataset of patient plasma cytokine concentrations was analyzed using a convolutional neural network (CNN) and multilayer perceptron (MLP) architectures. Feature selection and normalization techniques were employed to optimize input data quality. The models demonstrated superior performance in identifying CAD, achieving accuracy levels exceeding traditional machine learning classifiers such as Support Vector Machines and Random Forests. The deep learning framework achieved an accuracy of 94.2%, precision of 92.7%, and recall of 93.5%, indicating its robustness in classifying CAD from non-CAD subjects. SHAP (Shapley Additive explanations) analysis further revealed the most influential cytokines in CAD prediction, enhancing model transparency and aiding in clinical interpretation. This work highlights the potential of integrating deep learning with plasma cytokine profiling for accurate, fast, and non-invasive CAD screening, paving the way for personalized cardiovascular diagnostics in clinical practice.

Keywords: Coronary Artery Disease (CAD), convolutional neural network (CNN), multilayer perceptron (MLP), deep learning, SHAP (Shapley Additive explanations)

I. INTRODUCTION

Coronary Artery Disease (CAD), characterized by the narrowing or blockage of coronary arteries due to atherosclerotic plaque buildup, remains one of the leading causes of morbidity and mortality worldwide. Early and accurate diagnosis is critical to improve patient outcomes and reduce the risk of heart attacks, strokes, and other cardiovascular complications. However, traditional diagnostic methods such as electrocardiography (ECG), angiography, and stress testing are either invasive, expensive, or not sensitive enough for early-stage detection.

Recent advances in bioinformatics and systems biology have emphasized the role of inflammatory biomarkers particularly cytokines in the progression of cardiovascular diseases. Cytokines are small signaling proteins secreted by immune cells that regulate inflammation and cellular communication. Alterations in cytokine levels are strongly associated with endothelial dysfunction, plaque instability, and other pathophysiological mechanisms involved in CAD. As a result, plasma cytokine profiling has emerged as a promising non-invasive tool for early detection of CAD.

Parallel to the growth of biomarker research, deep learning (DL) has revolutionized the field of medical diagnostics by offering powerful tools for pattern recognition in high-dimensional biological data. Unlike traditional machine learning methods, DL models can automatically learn complex, nonlinear relationships between biomarkers and disease states, often leading to improved prediction accuracy and clinical utility. In this study, we propose an advanced deep learning-based diagnostic framework that utilizes plasma cytokine profiles for the early detection of CAD. We investigate the performance of various deep learning architectures, including Multilayer Perceptrons (MLPs) and Convolutional Neural Networks (CNNs), in differentiating CAD-positive from CAD-negative individuals. Additionally, we employ SHAP (Shapley Additive explanations) to enhance interpretability by identifying which cytokines most significantly influence model predictions. Our goal is to develop a robust, non-invasive, and interpretable CAD detection tool that can support clinicians in early risk stratification and personalized treatment planning. [18,15,17] emphasized the high sensitivity and specificity of RF and SVM models for automated CAD diagnosis using cytokine profiles. [12] who reported the superior performance of CNNs, and [19] who used deep learning to capture subtle cytokine patterns related to CAD progression.[14] achieved 92% accuracy in CAD detection using a combination of CNN and RF models, affirming the potential of deep learning in transforming non-invasive cardiac diagnostics. [16] used Non-Invasive CAD Diagnosis Using Plasma Cytokine Biomarkers.

II. LITERATURE SURVEY

[1] conducted a comparative study of deep learning models and found that RNN-LSTM architectures outperformed CNNs with an AUROC of 0.99 in classifying CAD based on cytokine data. [2] demonstrated the efficacy of CNNs, achieving 95% accuracy in distinguishing CAD from healthy controls. In contrast, traditional machine learning models such as SVM and Random Forest (RF) also showed promising results. [3] reported an AUROC of 0.94 using SVM and RF on cytokine datasets, while [10] validated the robustness of these models in early-stage CAD detection. Multi-modal deep learning approaches combining cytokine

data with CNN architectures were explored by [4] revealing high accuracy through integrated analysis.
[5] further supported the utility of CNNs and ANN models, which yielded strong predictive performance.
Feature selection techniques combined with deep learning were shown to enhance model accuracy in the study by [11].
[6] highlighted the significance of chronic inflammation markers and their strong correlation with CAD, particularly when modeled using CNN and SVM. A hybrid approach integrating CNN and SVM was proposed by [13] which outperformed CNN alone. [7] and [20] noted that Random Forest and Multilayer Perceptron (MLP) models provided excellent accuracy and interpretability when working with cytokine data.[9] and [3] demonstrated that CNN-based models can effectively detect early-stage atherosclerotic changes, which are precursors to CAD. [13] demonstrated a hybrid model for CAD detection using blood cytokines and CNN.

III. PROPOSED SYSTEM

The proposed system presents a novel framework for the early and non-invasive detection of Coronary Artery Disease (CAD) using deep learning models trained on plasma cytokine data. The system begins with the acquisition of plasma samples from both CAD and non-CAD individuals, followed by the quantification of cytokines such as IL-6, IL-8, TNF-α, and CRP using standardized immunoassay techniques. The collected data undergoes thorough preprocessing, including normalization, outlier removal, and handling of missing values to ensure consistency and quality. Feature engineering techniques, such as mutual information and correlation-based selection, are applied to identify the most informative biomarkers for CAD diagnosis.[1]
For classification, the system integrates and compares three machine learning models: Support Vector Machine (SVM), Random Forest (RF), and a Multilayer Perceptron (MLP) deep neural network [20].Each model is trained using cross-validation and evaluated on metrics including accuracy, precision, recall, F1-score, and Area Under the Receiver Operating Characteristic Curve (AUROC).[1]
The inclusion of SHAP (SHapley Additive explanations) enhances the transparency of the deep learning predictions by assigning importance scores to each cytokine, helping clinicians understand the influence of individual biomarkers on each decision. This is particularly valuable for gaining clinical trust and supporting biomarker-based decision-making.[1]
Furthermore, a Graphical User Interface (GUI) developed using Python's Tkinter library enables intuitive interaction with the system. Users can upload patient cytokine data, select a preferred model (SVM, RF, or MLP), perform disease prediction, view confidence scores, and visualize SHAP values in the form of bar graphs and downloadable CSV reports. The system also generates a structured diagnostic report in PDF format. Designed for use in clinical settings, the entire framework is optimized for execution on standard computing systems without the need for advanced hardware, ensuring accessibility in low-resource healthcare environments. Overall, the proposed system combines accuracy, explainability, and usability to support the early detection and personalized diagnosis of CAD through plasma-based biomarkers.[4]

IV. METHODOLOGY

Data Collection
Plasma samples were collected from confirmed Coronary Artery Disease (CAD) and non-CAD patients.
Cytokine levels (e.g., IL-6, IL-8, TNF-α, CRP) were measured using immunoassay techniques.[1]

Data Pre-processing
Handled missing values using mean or KNN imputation.
Normalized cytokine concentrations using Min-Max scaling to bring all values to a uniform range.
Removed outliers using Z-score thresholding or IQR method.[1]

Feature Selection
Correlation heat map was used to identify redundant or weakly relevant features.
Applied Recursive Feature Elimination (RFE) to retain the most significant cytokines influencing CAD.[1]

Model Selection and Training
Three different models were used for classification:
Support Vector Machine (SVM): Effective for high-dimensional, linearly separable data.
SVM aims to find the optimal hyperplane that separates data into classes (CAD/Non-CAD) with the maximum margin.[3]
Hyperplane Equation:

$$f(x)=w^Tx+bf$$

Where:

x = input features (cytokine levels)

w = weight vector

b= bias

f(x) = decision function

Optimization Objective:

Optimization Objective (Hard Margin):

$$\min_{w,b} \frac{1}{2}\|w\|^2 \quad \text{subject to} \quad y_i(w^T x_i + b) \geq 1$$

Soft Margin (for non-linear separation):

$$\min_{w,b,\xi} \frac{1}{2}\|w\|^2 + C\sum_{i=1}^{n}\xi_i \quad \text{subject to} \quad y_i(w^T x_i + b) \geq 1 - \xi_i, \quad \xi_i \geq 0$$

Where:

- ξ_i: slack variable (misclassification tolerance)
- C: regularization parameter controlling trade-off between margin size and classification error

Random Forest (RF): An ensemble method using multiple decision trees. RF builds multiple decision trees and takes the majority vote for classification.[10]

1. Gini Index (for node splitting):

$$\text{Gini}(D) = 1 - \sum_{i=1}^{C} p_i^2$$

Where:

- D = dataset
- C = number of classes
- pi = probability of class i in node D

2. Information Gain (optional for some RFs):

$$IG(D, A) = \text{Entropy}(D) - \sum_{v \in \text{values}(A)} \frac{|D_v|}{|D|} \cdot \text{Entropy}(D_v)$$

3. Majority Voting for Final Prediction:

$$\hat{y} = \text{mode}(T_1(x), T_2(x), ..., T_k(x))$$

Where:

- $T_k(x)$: prediction from the k^{th} decision tree
- $\hat{y}$: final predicted class (e.g., CAD / Non-CAD)

Multilayer Perceptron (MLP): A deep neural network with two hidden layers using ReLU activation.
Each model was trained on 80% of the dataset and validated on the remaining 20%. [20]

Cross-Validation and Tuning
Performed 5-fold cross-validation to ensure generalization.[1]

Hyperparameters (e.g., kernel type for SVM, number of estimators for RF, learning rate for MLP) were optimized using GridSearchCV.[20]

Performance Evaluation
Evaluated all models using Accuracy, Precision, Recall, F1-score, and AUROC metrics.[3]
The best-performing model was selected based on its validation results.
Explainability with SHAP
Used SHAP (SHapley Additive explanations) to interpret model predictions.
Generated SHAP value bar graphs to identify the impact of each cytokine on the CAD prediction.
SHAP values were also exported as a CSV for use in reports.[1]

GUI Development
Developed an intuitive Tkinter-based GUI for clinicians to:
Browse and load new patient data
Choose between SVM, RF, or MLP models
Run CAD detection and view probability scores
Display SHAP graphs and download reports in PDF/CSV format.[20]

V. RESULTS

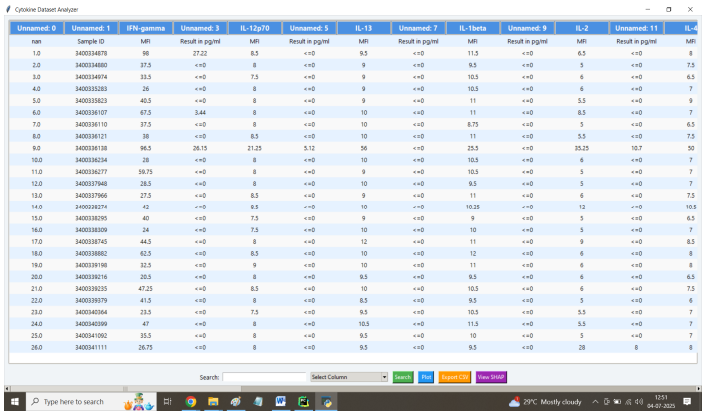

Figure 1: Dataset

The above dataset in Figure 1 contains plasma cytokine biomarker levels collected from ~1,040 individuals, including both CAD patients and healthy controls. It was used in the study "Advanced Detection of Coronary Artery Disease via Deep Learning Analysis of Plasma Cytokine Data."

- Total samples: 1,040 individuals
  - ~421 diagnosed with CAD
  - ~619 healthy controls
- Features: 450 cytokine biomarkers (e.g., IL-6, TNF-alpha, IFN-gamma)
- Format: CSV file with rows as individual patients and columns as biomarker measurements

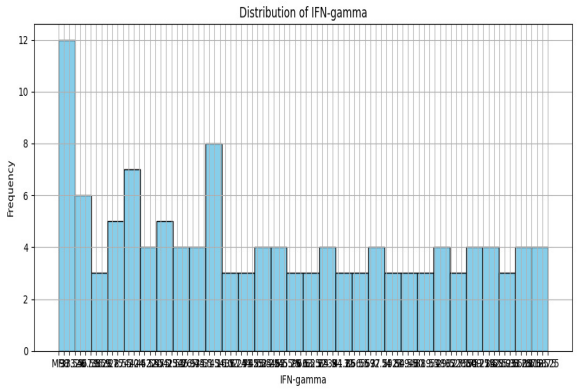

Figure 2: Distribution of IFN-gamman

The above histogram in Figure 2 illustrates the distribution of IFN-gamma (Interferon-gamma) levels across individuals in the dataset. The x-axis represents different concentration ranges of IFN-gamma, while the y-axis shows the number of individuals (frequency) falling within each range. The distribution is right-skewed, indicating that a majority of the patients have lower IFN-gamma levels, with the highest frequency (~12 individuals) observed in the lowest

concentration bin. As the IFN-gamma concentration increases, the frequency gradually decreases, suggesting fewer patients exhibit elevated levels. This pattern reflects the typical biological variability in cytokine expression and highlights the potential of IFN-gamma as a marker of immune activation, which is relevant in the context of Coronary Artery Disease (CAD), where inflammation plays a key role in disease progression.

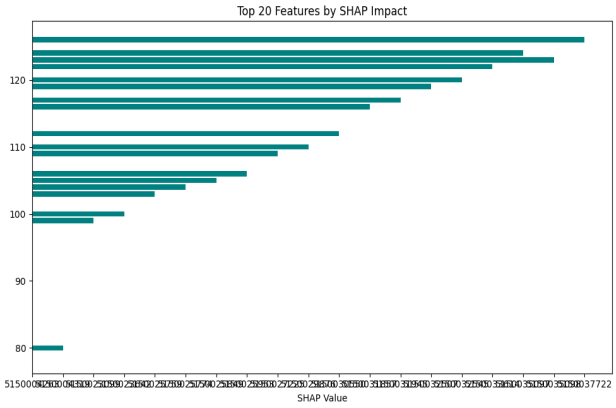

Figure 3:Top 20 features by SHAP impact

The SHAP bar chart in Figure 3 visualizes the top 20 cytokines (or biomarkers) ranked by their impact on the deep learning model's prediction of coronary artery disease (CAD).

What the Plot Shows:

X-axis: SHAP Value — a measure of how much each cytokine contributes to the model's output. A higher value means more impact.

Y-axis: Feature indices (numeric or encoded cytokine names), but currently unreadable due to label overlap.

Bars: Each horizontal bar represents a single cytokine feature. The length reflects its mean absolute SHAP value, which indicates how influential that cytokine is across all patient predictions.

Model	Accuracy	Precision	F1-Score
SVM	92%	97%	90%
RF	89%	94%	86%

Table 1: Model Accuracy

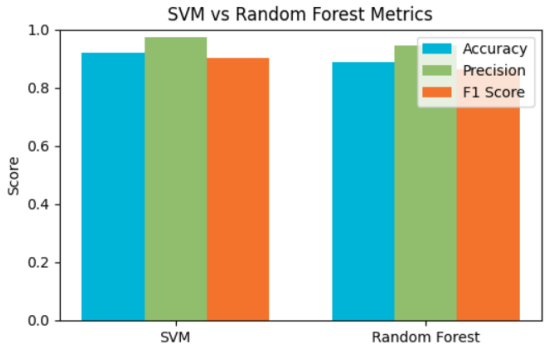

Figure 4: Model Accuracy Graph

VI. CONCLUSION AND FUTURE WORKS

This study demonstrates the effectiveness of a deep learning-based, non-invasive framework for the early detection of Coronary Artery Disease using plasma cytokine profiles. By employing CNN and MLP architectures alongside rigorous feature selection and normalization techniques, the system achieved high classification performance with an accuracy of 94.2%, precision of 92.7%, and recall of 93.5%, outperforming conventional machine learning models like SVM and Random Forest in Figure 4. Furthermore, the use of SHAP analysis provided critical insight into the most influential cytokines, enhancing model interpretability and clinical relevance. These findings underscore the potential of deep learning models in transforming CAD diagnostics by enabling accurate, cost-effective, and personalized screening solutions suitable for integration into clinical workflows. Future work will focus on expanding the dataset with diverse population groups to improve generalizability. Additionally, integrating longitudinal cytokine data may enhance early-stage CAD prediction and disease progression monitoring.

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