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APPLIED RESEARCH

Prediction of Blood Glucose Concentration Based on OptiScanner and XGBoost in ICU

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ABSTRACT Hyperglycemia, a stress-induced physiological condition, is associated with severe complications, including sepsis, multiple organ failure, and higher mortality rates. The seminal 2001 Leuven study highlighted the potential for strict blood glucose control (80-110 mg/dL) to lower mortality rates by 34% among critically ill surgical patients. Consequently, monitoring blood glucose levels in ICU patients has become imperative. This study aims to use recent medical technology advancements to streamline the monitoring of blood glucose levels, traditionally requiring trained personnel to operate a blood glucose monitor. We used the OptiScanner to collect patient blood data, separate plasma, and acquire mid-IR-related data. XGBoost was used to improve the prediction of blood glucose concentration based on patient classification types and its performance was compared with two other machine learning algorithms. We also used the LASSO model to predict plasma blood glucose concentrations. Additionally, we applied SHAP (SHapley Additive exPlanations) to identify critical wavelengths in the classifier and compared these with the functional groups corresponding to the actual IR spectrum. Our experimental findings demonstrate that XGBoost exhibits promising performance. Furthermore, the interpretation of the model is in alignment with domain knowledge. Through this study, we emphasize the potential of advanced medical technology, particularly machine learning algorithms such as XGBoost, to improve the efficacy and precision of blood glucose monitoring in ICU settings.

INDEX TERMS Hyperglycemia, blood glucose monitoring, OptiScanner, XGBoost, machine learning, LASSO model, SHAP, infrared spectrum, intensive care.

I. INTRODUCTION

Diabetes, a chronic disease that affects the way the body converts food into energy, is one of the leading causes of death worldwide [1]. Implementing a strategy for tight glycemic control is crucial to reduce the risk of diabetes-related complications, such as coronary heart disease and ischaemic stroke [2], [3]. Alongside a healthy diet, continuous monitoring of blood glucose is essential, making self-monitoring of patient blood glucose levels at home important [4]. Various devices, including handheld glucometers and continuous glucose monitoring devices, have been developed to facilitate home-based glucose monitoring.

Evidence supports that appropriate methods for glucose monitoring improve the quality of life of patients. Several studies have highlighted the importance of glycemic control in intensive care unit (ICU) patients, associating strict glucose control protocols with improved survival rates [5]. Thus, research on the definition of healthy glucose ranges is of great importance [6]. However, tight glucose control necessitates precise, frequent sampling and prompt availability of reliable results. Unfortunately, few methods offer accurate routine point-of-care glucose level measurements in the ICU. The use of handheld meters has demonstrated inaccuracies [7] and requires the assistance of nursing staff, which could lead to a reduced collection frequency due to time constraints [8]. On the contrary, real-time automated continuous glucose monitoring systems (CGMS) can accurately detect glucose

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concentration every few minutes [9]. Furthermore, CGMS can be integrated with insulin automation devices to regulate insulin delivery and shut-off at predefined glucose levels [10].

Machine learning (ML) techniques have become indispensable in various industries [11], [12], with applications ranging from computer vision and natural language processing to biological studies [13], [14], [15]. Central to ML's efficacy is its capability to autonomously derive predictive models from data while handling complex or high-dimensional data types without assuming an underlying data distribution. This adaptability makes ML increasingly valuable in instrumental analysis, which explains its growing adoption in recent years [16], [17], [18].

On the other hand, mid-infrared (mid-IR) spectral technology employs the principle of infrared light absorption to detect changes in the vibrations of covalent bonds. These changes, specific to different molecules, allow the detection and quantification of glucose within the mid-IR region [19]. Furthermore, mid-IR spectral technology has demonstrated significant potential in identifying plasma components [20]. To exploit this potential, we utilize data collected through OptiScanner, a mid-IR spectroscopy tool connected to an existing blood access port for patients in the ICU, to develop predictive models.

In this paper, we use the strengths of ML in conjunction with mid-IR spectral technology to predict blood glucose concentrations. However, a notable drawback of ML is the opacity of its algorithms; many function as ''black-box'' models, making it challenging for practitioners to understand the rationale behind model predictions. This lack of interpretability hinders the seamless deployment of ML models in production environments, thus underscoring the importance of research into explainable AI (XAI).

However, there is a trade-off between model accuracy and explainability in ML. Highly accurate models typically involve intricate, non-linear transformations, whereas more straightforward, linear models often fail to deliver accurate predictions for most complex problems. To address this issue, our work advocates using post hoc explainability techniques to elucidate the predictions made by the developed ML model.

Our research focuses on training ML models, including Partial Least Squares Regression (PLS) [21], Lasso [22], and XGBOOST [23], to predict plasma glucose levels. We extend our model development to include patients treated with hetastarch, an agent used to prevent hypovolemia (a condition marked by decreased blood plasma volume, also known as ''shock''). To improve the accuracy of concentration predictions, we construct ML models, such as the support vector machine (SVM) [24], XGBOOST, random forest [25], logistic regression [26], and K nearest neighbor (KNN) [27], aiming to distinguish between regular ICU patients and those treated with hetastarch. Finally, we employ SHAP [28] to elucidate the relationships between chemical structures and key features identified by our model.

The contributions and novel aspects of this paper are as follows:

1) We innovatively integrate mid-IR spectral technology with ML algorithms to achieve precise prediction of glucose levels in ICU settings.
2) Our work extends existing model development by incorporating patients treated with hetastarch, offering a more comprehensive predictive model.
3) We implement post hoc explainability techniques to provide insights into the ''black-box'' nature of ML algorithms, effectively bridging the gap between model accuracy and interpretability.

II. RELATED WORK

Diabetes mellitus is a complex endocrine disorder characterized by elevated blood glucose levels, leading to various complications such as heart disease, stroke, and dementia. Therefore, strict glycemic control is essential for effective diabetes management, making continuous monitoring of blood glucose crucial for patients.

Nie et al. [29] explored non-contact blood glucose detection through imaging photoplethysmography (IPPG). They used a near-infrared camera to capture facial videos and extracted 26 time-domain features from the IPPG signals. Four ML algorithms, including principal component regression (PCR), partial least-squares regression (PLS), support vector regression (SVR), and random forest regression (RFR), were used for predictive modeling. Their results highlighted RFR as the most accurate method. Similarly, Alfian et al. [30] devised a blood glucose prediction model for Type 1 diabetes (T1D) using time-domain features. Testing the model on 12 patients with T1D showed that Artificial Neural Networks (ANNs) yielded the best results.

Personalization in blood glucose prediction is crucial due to patient-to-patient variations. However, collecting sufficient patient-specific data for model training is both challenging and expensive. To address this, Daniels et al. [31] introduced a multi-task learning approach using hard parameter sharing techniques. The model architecture comprises shared, clustered, and individual-specific layers. Shared layers are trained on aggregated data from all subjects, while individual-specific layers use data from particular subjects. Clustered layers, situated between shared and individual-specific layers, aim to group individuals according to their glycemic variability.

Predicting near-future glucose levels is of significant importance. Martinsson et al. [32] utilized recurrent neural networks to forecast blood glucose levels up to an hour in advance. Distinctively, their study relied exclusively on historical glucose level data from individual patients for model training. While this approach simplifies data collection, it neglects other potentially valuable information, such as demographic data. Gómez-Castillo et al. [33] advocated using Long Short-Term Memory (LSTM)) [34] networks to predict future glucose levels. Their model was trained

on the OhioT1DM database, which consists of eight weeks of continuous glucose monitoring, insulin administration, physiological sensor data, and self-reported life events for each of the 12 individuals with T1D [35]. The study yielded promising results in predicting glucose levels.

Ensemble learning methods, which combine multiple ML algorithms, have also been explored for their potential to improve predictive performance. Saiti et al. [36] integrated several glycemia prediction algorithms using three ensemble methods: linear, bagging, and boosting. For small datasets, their results indicated that a bagging meta-regressor outperformed individual algorithms across all prediction horizons. Furthermore, Nemat et al. [37] used a stacking approach, combining linear models, vanilla LSTM [34], and bidirectional LSTM, to predict blood glucose levels in patients with T1D. Their ensemble models showed superior performance compared to non-ensemble benchmarks.

III. PRELIMINARY

Infrared (IR) spectroscopy is a powerful analytical technique that examines the interactions between infrared radiation and matter through mechanisms such as absorption, emission, or reflection. The infrared spectrum covers wavenumbers ranging from approximately 12,800 to 10 cm^{-1} and wavelengths from 0.78 to 1,000 μm. Depending on the application and instrumentation, the IR spectrum is generally divided into three sub-regions, as outlined in Table 1: near-IR, mid-IR, and far-IR.

TABLE 1. IR spectral regions.

Region	Wavelength, μm	Wavenumbers,cm^{-1}
Near	0.78 to 2.5	12800 to 4000
Middle	2.5 to 50	4000 to 200
Far	50 to 1000	200 to 10

Mid-infrared spectroscopy, a common spectroscopic technique, is based on molecular interactions with electromagnetic radiation in the mid-infrared region. It enables the exploration of fundamental vibrations and associated rotational-vibrational structures of chemical bonds. Yu et al. [19] proposed a minimally invasive method to measure glucose concentration using mid-IR spectroscopy, paired with a tunable carbon dioxide (CO2) laser and a compact fiber-based ATR sensor. Kasahara et al. [20] developed a non-invasive blood glucose measurement method using mid-infrared absorption spectroscopy, employing specific wavenumbers to measure blood glucose concentration.

IV. MATERIALS AND METHODS

A. DATA

The dataset used in this experiment originates from glucose concentration measurements from ICU patients, comprising 25 wavelength bands ranging from 7 to 10 μm and associated labels. The glucose concentration of each patient was determined by a blood test using the YSI STAT 2300. This device employs a steady-state measurement methodology in which glucose oxidase, embedded in a membrane, catalyzes the conversion of glucose into gluconic acid and hydrogen peroxide.

Due to privacy regulations and the sensitive nature of the data used in this study, the raw data cannot be publicly accessible. Data were used under license for the current study. Data are, however, available from the authors upon reasonable request and with the permission of the original data source. The research team has ensured that all results presented in this paper are reproducible based on the processed data, methodologies, and statistical analyzes detailed in the text. In addition, the authors declare that they have no conflict of interest with the content of this article. The code pertinent to this study has been made publicly accessible on GitHub.[1]

The OptiScanner, an automated plasma-based bedside glucose monitoring system equipped with mid-IR spectroscopy, collected glucose wavelength information. This system specifically utilizes 25 spectral bands between 7 to 10 μm within the mid-IR range, as this longer wavelength range yields sharp and pronounced glucose peaks [38]. The spectral measurement method involves introducing the blood sample into a cuvette which is then positioned between a light source and a detector. To expose the sample to specific wavelengths, the full spectrum of light from the source is filtered by an optical filter. Finally, the detector will receive the transmitted light.

In our dataset, the label differentiates patients who received hetastarch treatment, since its usage alters the composition of the blood. It is important to recognize that blood, a cocktail of numerous components, contributes to the spectrum at all wavelengths; hence, no single wavelength in the blood spectrum can predict glucose concentration. According to patient-specific conditions, medical professionals administered hetastarch to certain patients in the ICU.

B. XGBOOST

This section briefly discusses the XGBoost algorithm, a widely recognized ensemble learning method based on gradient boosting. The objective function of XGBoost is to minimize the loss term and a regularization term to prevent overfitting. The algorithm trains additively and iteratively refines the predictions.

XGBoost employs the second-order Taylor expansion to approximate the objective function, helping in efficient optimization. The algorithm also incorporates gradient and Hessian information for each data point and uses them to calculate optimal leaf weights. Moreover, XGBoost deploys regularization terms that control the complexity of the individual trees in the ensemble. This results in a scoring function that allows a greedy algorithm to determine the

[1]Repository Link: https://github.com/clliu168/Blood-Glucose-Concentration-Prediction

optimal tree structure. Following a series of equations, Eq. (1) shows the scoring function to measure the quality of a tree structure q. For a detailed mathematical formulation of XGBoost, we refer the reader to the seminal paper by Chen and Guestrin [23].

$$\hat{\mathcal{L}}^{(t)}(q) = -\frac{1}{2}\sum_{j=1}^{T}\frac{(\sum_{i\in I_j} g_i)^2}{\sum_{i\in I_j} h_i + \lambda} + \gamma T. \tag{1}$$

Here, g_i and h_i symbolize the gradient and Hessian of the loss function, respectively, γ and λ are hyperparameters that control the weights of these two regularization terms. Furthermore, we introduce I_j to denote data samples classified into leaf j and T is the number of leaves in the tree.

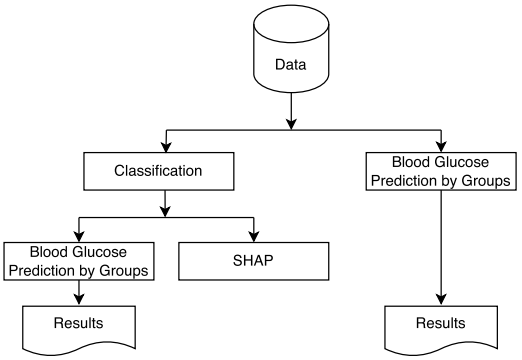

FIGURE 1. Research flow.

C. RESEARCH PROCESS

This paper uses patient blood wavelength data in the ICU acquired via the OptiScanner, a mid-IR spectroscopy device. This research aims primarily to leverage these data to predict glucose concentration levels. In particular, ICU medical professionals use hetastarch to treat hypovolemia, a condition that may result from severe trauma, including significant blood loss. However, the use of hetastarch could affect the prediction of glucose concentration. Hence, our interest lies in discerning whether glucose concentration predictions could be improved by distinguishing patients who have received hetastarch. Experimental procedures are then carried out to compare glucose concentration results with and without this patient classification.

Our proposed methodology consists of two primary stages. Initially, a model is trained using the designated training set, following which the test set is used to evaluate the model. The prediction results and associated labels are subsequently analyzed to generate a confusion matrix. The second stage involves the creation of regression models tailored to the various labels of the training set. The performance of each of these models is then verified using the test set. The workflow of our proposed methodology and the baseline approach for comparison are depicted in Figure 1.

For the classification task, a variety of ML algorithms are used, including logistic regression (LR), random forest (RF), XGBoost (XGB), support vector machine (SVM), and K nearest neighbor (KNN). In terms of regression, methods such as random forest (RF), LASSO, and partial least-squares regression (PLS) are utilized. Through these algorithms, we conduct experiments comparing the performance of these methods to identify the most appropriate prediction model for the given dataset. Additionally, all algorithmic model parameters are optimized using grid search. For evaluating model performance, we use the confusion matrix to compute the accuracy of the classification models and the root mean square error (RMSE) for assessing the regression models. The RMSE is defined as the square root of the average of squared differences between predicted results and actual observations. The definition of RMSE is listed in Eq. (2), where y_i and $\hat{y}_i$ are ground truths and predictions, respectively.

$$RMSE = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(y_i - \hat{y}_i)^2} \tag{2}$$

In addition to experimental results, we employ the SHAP (SHapley Additive exPlanations) method [28] to explain our model's predictions. SHAP derives from coalitional game theory and calculates Shapley values to estimate the contribution of each feature to a given instance's prediction, x. This approach significantly differs from traditional feature importance measures, which merely indicate influential features without providing an in-depth explanation. Instead, SHAP provides a more comprehensive analysis, providing both positive and negative relationships between predictors and the target variable. This enhanced understanding aligns with practical business practices and offers insights into why each case obtains its specific prediction, based on its unique predictor values.

V. RESULTS

A. CLASSIFICATION

Our study included a total of 1021 patients. We separated the patients into training and test sets. The training set comprises 523 patients in the normal ICU and 110 with hetastarch. On the other hand, the test set has 356 patients in the normal ICU and 32 with hetastarch.

Initially, we trained five distinct classification models. Subsequently, we compared the performance of these five models based on the accuracy derived from the confusion matrix. The accuracy can be formulated using elements of the confusion matrix as shown in Eq. (3).

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}. \tag{3}$$

Here, TP refers to the true positives, which are the correctly predicted positive values. TN refers to true negatives, representing correctly predicted negative values. FP stands for false positives, indicating negative instances incorrectly classified as positive. Finally, FN represents false negatives, meaning positive instances that are incorrectly classified as negative. This matrix offers a comprehensive view of the model's accuracy while providing details about the actual

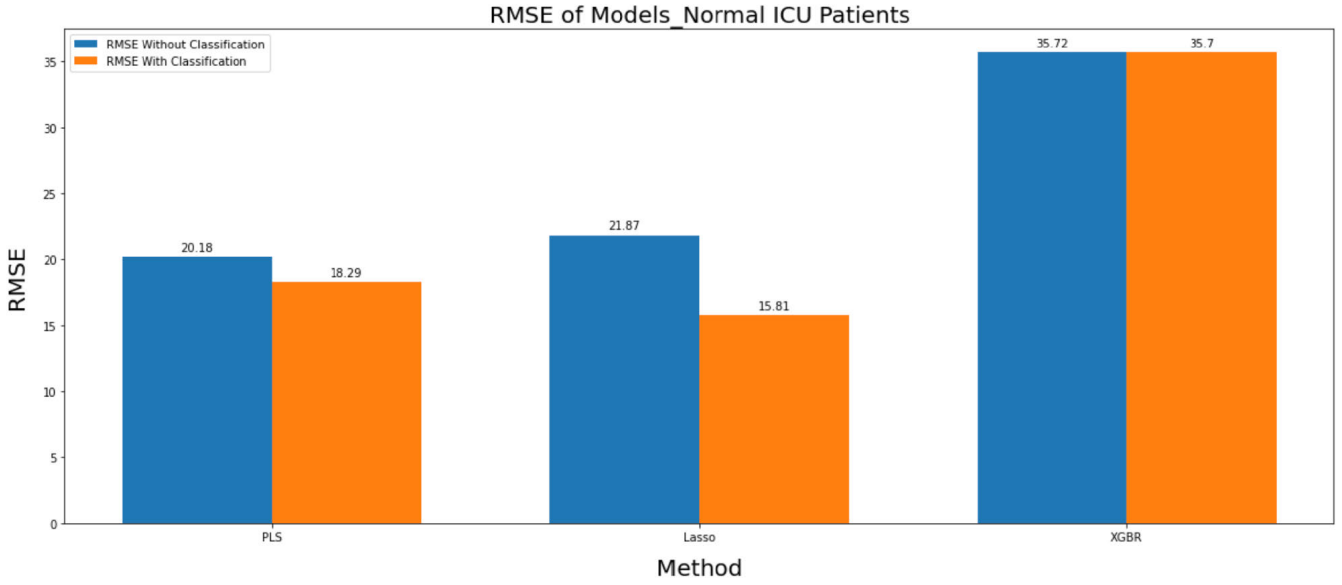

FIGURE 2. Experiment results for normal ICU patients.

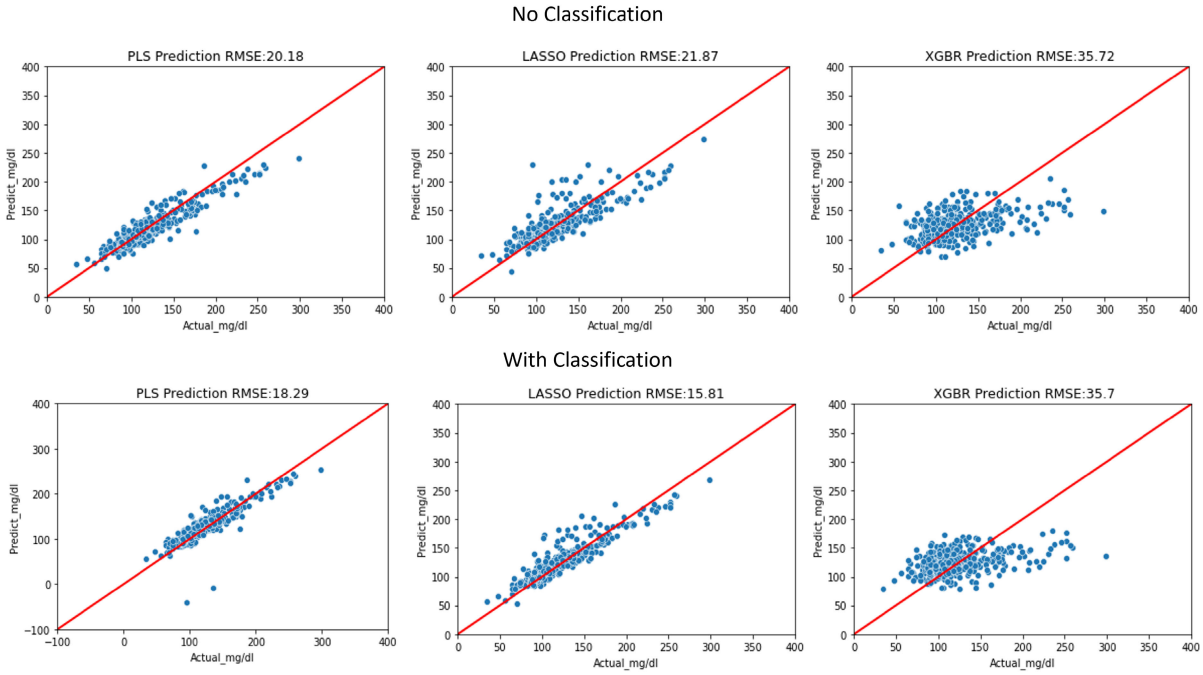

FIGURE 3. Scatter plots of predicted glucose concentrations and reference glucose concentrations for normal ICU patients without/with classification.

and predicted classes. We utilize the training set for model training and hyperparameter tuning and perform a five-fold cross-validation. The results are illustrated in Table 2.

B. REGRESSION

Furthermore, we trained ML models to predict plasma glucose concentration, including PLS, Lasso and XGBoost regression. To verify our hypothesis that implementing classification is superior to not using classification, we first trained models on a non-classified training set and evaluated their performance using the validation set. Subsequently, these results were compared to the performance of models trained in a classified training set and evaluated in a classified validation set.

Fig. 2 demonstrates that implementing classification first improves the accuracy of the glucose concentration prediction in standard ICU patients. Fig. 3 presents the scatter plots and the fitting lines of the predicted glucose concentrations

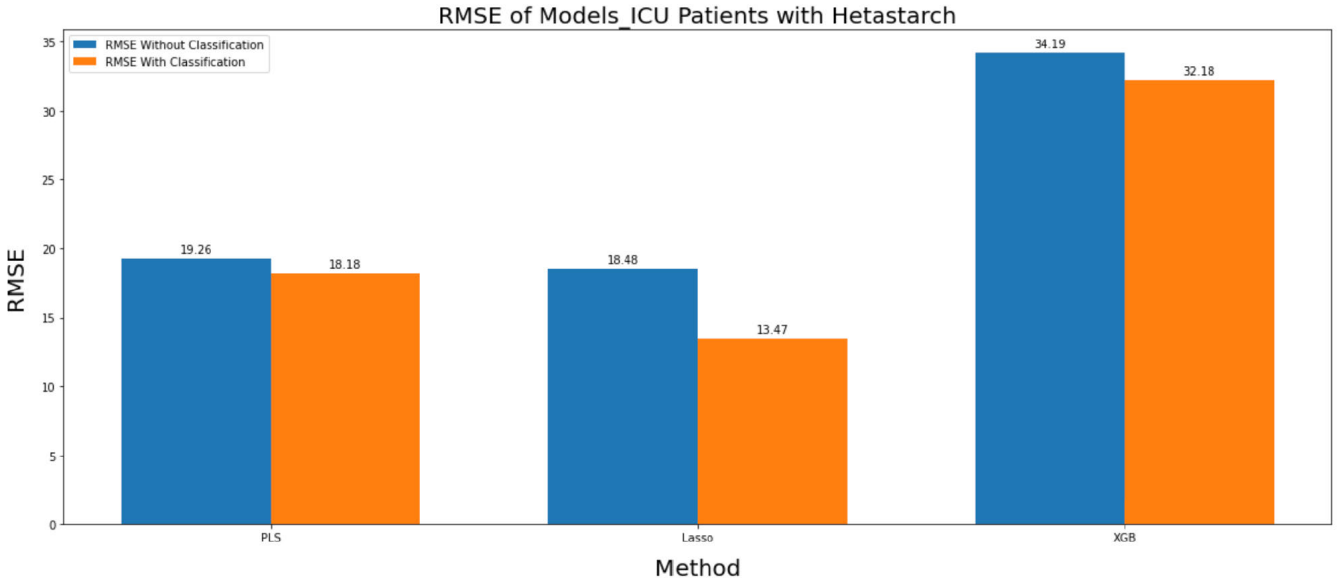

FIGURE 4. Experiment results for ICU patients treated with hetastarch.

TABLE 2. The performance of various classification models with testing set.

Algorithm	Accuracy
SVM	99.48 %
XGBOOST	100.00%
Random Forest	100.00%
Logistic Regression	99.74%
KNN	98.97%

versus the reference glucose concentrations in standard ICU patients.

In line with these observations, Fig. 4 indicates that first performing classification improves the accuracy of glucose concentration prediction in ICU patients treated with hetastarch. Furthermore, Fig. 5 shows the scatter plots and the fitting lines of predicted glucose concentrations versus reference glucose concentrations in patients in the ICU treated with hetastarch.

VI. DISCUSSION

A. SHAPLEY ADDITIVE EXPLANATION (SHAP)

This study focuses on identifying which fragment significantly impacts prediction results. To reveal the black box of the developed model, we proposed using SHAP (SHapley Additive exPlanations) [28] to explain and investigate the model results. The SHAP is a game-theoretic approach designed to explain the output of any ML model. It calculates the contribution of each feature to a specific instance's prediction, treating feature values of a data instance as players in a coalition. Shapley values then fairly distribute the ''payout'' among the features, assigning each feature an importance value for a specific prediction. SHAP has been extensively applied to various supervised learning models. For instance, Lin et al. [39] employed SHAP analysis to evaluate the impact of each feature on their classifier.

In particular, the SHAP value is capable of reflecting the influence of each feature on individual samples and indicates both their positive and negative effects. The global interpretability provides us with an understanding of the direction and numerical scale of each feature's impact on the predicted value. Fig. 6 shows the global feature importance, calculated by averaging the absolute Shapley values of each feature across the dataset and sorting the features in descending order of importance. Based on the magnitude of the feature attributions, it is clear that wavelength 3 is the most predictive variable for the trained XGBoost model.

Fig. 7 provides a summary plot showcasing the relationship between a feature's value and its impact on the prediction. Each point on the summary plot represents a Shapley value for a feature. As shown in Fig. 7, we deduce that wavelength 3 is the most important feature and has the most significant value of the feature to determine the prediction.

To perform further investigation, we turn our attention to individual predictions that were correctly determined. Fig. 8 and Fig. 9 both start from the same baseline value. The prediction originates from this baseline, and its Shapley values are the average of all predictions. Each Shapley value is depicted with an arrow, indicating an increase (positive value) or decrease (negative value) in the prediction. In Fig. 8, we observe that wavelength 3 mainly contributes negatively to predicting that the ICU patient did not receive

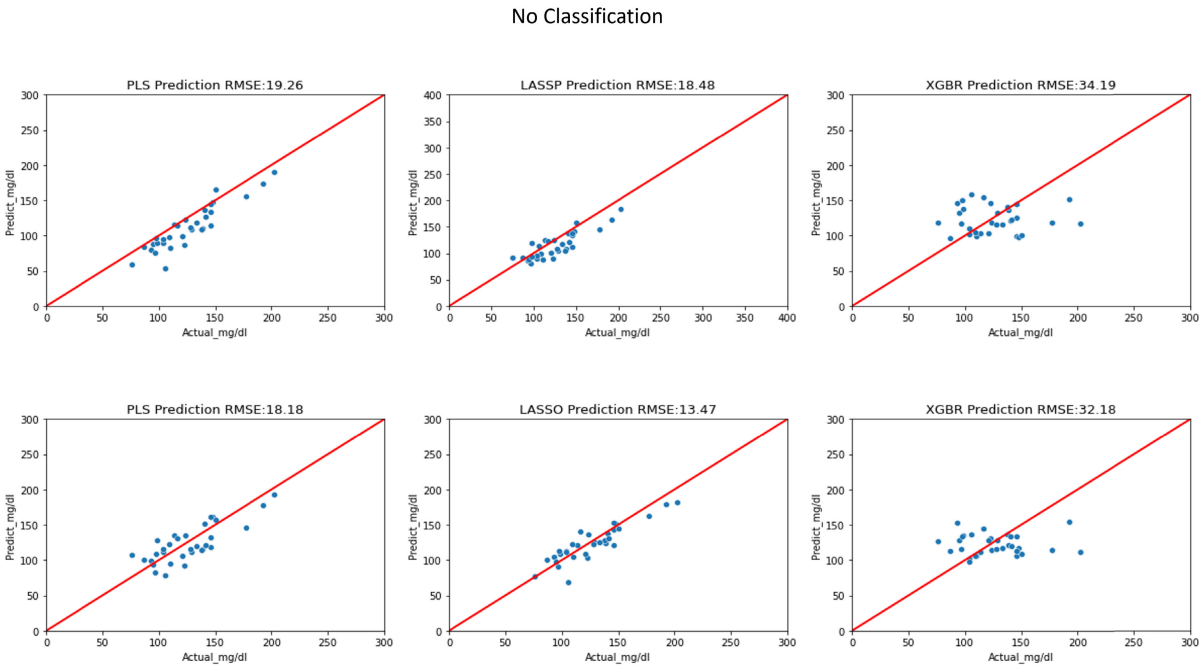

FIGURE 5. Scatter plots of predicted glucose concentrations and reference glucose concentrations for ICU patients treated with hetastarch without/with classification.

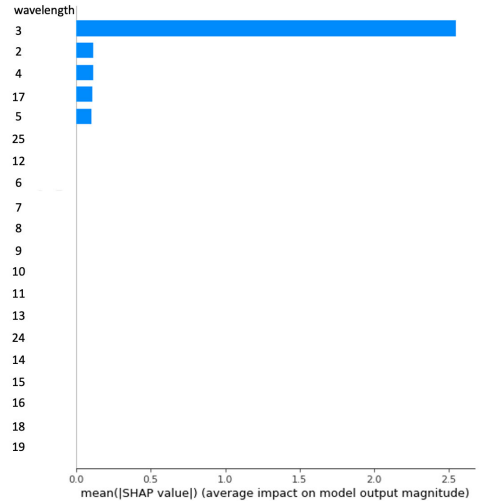

FIGURE 6. The average of the SHAP value of each feature, the wavelength3 was the most important feature.

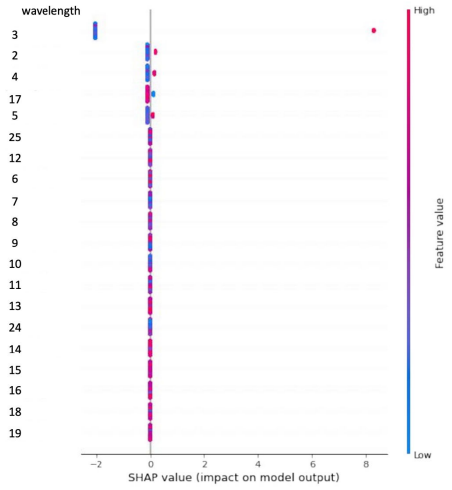

FIGURE 7. The summary plot indicates that Wavelength 3 is the most important feature and possesses the most significant feature value.

hetastarch treatment. On the contrary, wavelength 3 is a substantial positive contribution to predicting that the ICU patient received hetastarch treatment, as seen in Fig. 9. Upon an overall examination of the force plots, SHAP clustering is effective in grouping the Shapley values of each sample. As shown in Fig. 10, it is a commonality that wavelength 3 serves as a primary positive contribution in all ICU patients treated with hetastarch.

B. ANALYSIS

Our trained model identifies wavelength 3 as the most crucial feature, contributing significantly to the predictions it makes. In the mid-infrared (mid IR) range, wavelength 3 corresponds to a 7240nm wavelength, which can be converted to 1381.22 cm^{-1} in wavenumbers. Understanding the link between the chemical structure of hetastarch and the mid IR could explain why wavelength 3 is integral to our model's predictive capacity, given the known differences between two studied groups related to the use of hetastarch.

Investigating the Infrared (IR) Spectrum table in Table 3,[2] we observe that the OH bending of alcohol occurs within the mid-IR range, specifically between 1420 and 1330 cm^{-1}.

[2]IR Spectrum Table and Chart from Merck https://www.sigmaaldrich.com/TW/en/technical-documents/technical-article/analytical-chemistry/photometry-and-reflectometry/ir-spectrum-table

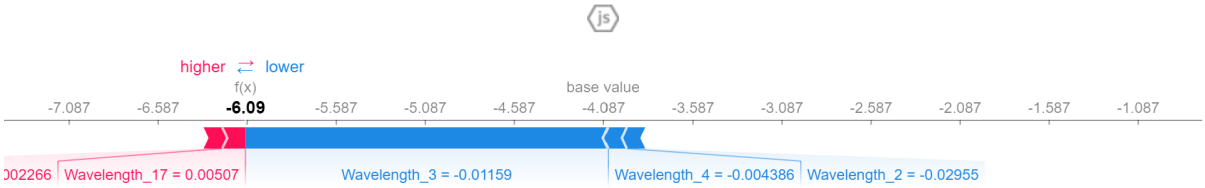

FIGURE 8. The sample 2: Correctly predicted the normal ICU patient was not treated with hetastarch.

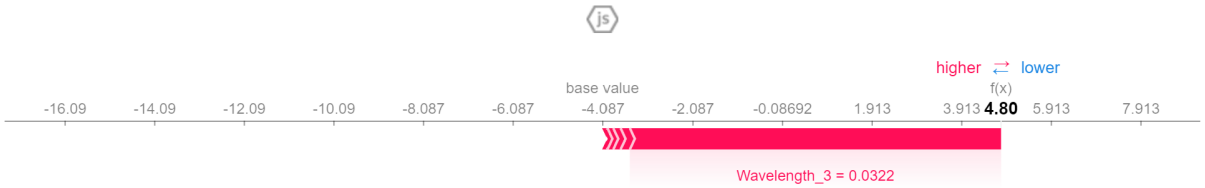

FIGURE 9. The sample 385: Correctly predicted the ICU patient was treated with hetastarch.

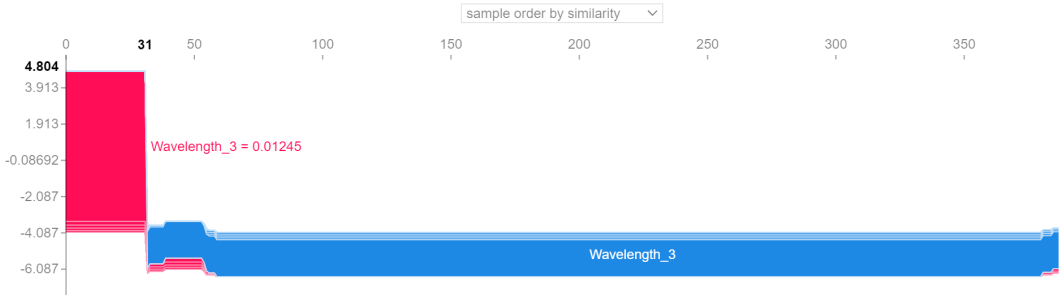

FIGURE 10. The stacked SHAP explanations clustered by explanation similarity.

The Fig. 11 reveals that the chemical structure of hetastarch contains numerous OH groups.[3]

TABLE 3. Function group.

Absorption,cm^{-1}	Group	Compound Class
1440-1395	O-H bending	carboxylic acid
1420-1330	O-H bending	alcohol
1415-1380	S=0 streching	sulfate
1410-1380	S=0 streching	sulfonyl chloride
1400-1000	C-F streching	fluoro compound
1390-1310	O-H bending	fluoro phenol

Ioppolo et al. [40] provided mid-IR crystalline spectra of the materials they studied. The OH-bend occurs at 7 um (1415 cm^{-1}) in the spectrum of CH_3OH, at 7.2 μm (1390 cm^{-1}) in the spectrum of HCOOH, and at 7.1 μm (1410 cm^{-1}) in the spectrum of CH_3COOH. The absorption of infrared light results in changes in a molecule's covalent bond vibrations.

[3]Hetastarch structure information from National Center for Biotechnology Information https://pubchem.ncbi.nlm.nih.gov/compound/Hydroxyethyl-starch

Therefore, we hypothesize that the importance of Wavelength 3 to the prediction stems from its sensitivity to the presence of numerous OH groups in hetastarch. These OH groups exhibit characteristic absorption within the mid-IR range from 1420 to 1330 cm^{-1}, which correlates with the predictive capabilities of our model.

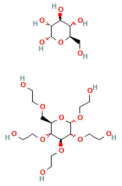

FIGURE 11. Using IR spectrum table to look for the frequency of Wavelength 3. Its frequency is 1381.22 cm^{-1} which correspond to OH group. Hetastarch equips many OH groups.

VII. CONCLUSION

This research aimed mainly to formulate a method capable of increasing the precision of glucose concentration predictions. Recognizing the frequent administration of hetastarch to certain patients in the Intensive Care Unit (ICU), it was imperative to integrate this factor into our

modeling framework. The absence of such categorization based on hetastarch treatment could potentially compromise prediction fidelity. To this end, we initially began to train a multitude of classification models designed to discern between patients who had received hetastarch and those who had not. Subsequently, the optimal model was selected for a detailed analysis using the SHAP method to elucidate the decision-making process embedded in the model. Our findings were then enriched by integrating insights drawn from extensive expertise in analytical chemistry, thereby offering a more comprehensive interpretation of the SHAP-derived explanations.

A. LIMITATIONS AND FUTURE WORK

While this study offers valuable insights into the predictive power of ML algorithms combined with Mid-Infrared (mid-IR) spectral technology for estimating blood glucose levels, some limitations warrant discussion.

1) Small Dataset: The study employs a relatively small dataset, which may impact the generalizability and objectivity of the results.
2) Limited Feature Set: Our feature set is highly focused on mid-IR spectral data and lacks additional information, such as height, weight, age, or relevant medical data. This absence of supplementary features constrains the scope of the research and could limit its adaptability to other domains or applications.

Future research could address this limitation by using more extensive and diverse datasets, thereby enhancing the robustness and applicability of the predictive models. Besides, it may be beneficial to incorporate a broader set of features beyond mid-IR data, including demographic and medical information. By doing so, researchers could explore how these additional variables influence the model's performance and potentially unlock new avenues for multidisciplinary research in the healthcare domain.

Within the scope of this research, our attention was primarily directed toward examining the influence of hetastarch on glucose concentration predictions, primarily due to the notable disparities in treatment protocols found in the ICU patient dataset. As a pathway for future exploration, our aim is to collate a more inclusive dataset that covers a wider spectrum of treatment parameters and specific patient traits. We believe that this would allow us to refine and further enhance the predictive accuracy of our glucose concentration models.

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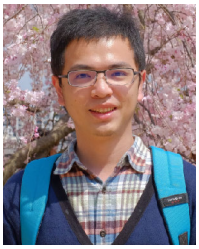

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