

# Development of Electrical Impedance Spectroscopy (EIS) Technique to Classify Diabetes Mellitus Disease Using Machine Learning with Backpropagation Method

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## Abstract

Diabetes mellitus is an urgent challenge for global health. According to data from the International Diabetes Federation (IDF), the prevalence of diabetes has increased significantly in the last 5 years and is predicted to reach 700 million cases by 2045. Recently, a diabetes screening method based on the electrical properties of cells using the Electrical Impedance Spectroscopy (EIS) technique was proposed. In previous studies, the EIS technique was only used to identify cell and tissue damage but was not yet able to classify a disease such as diabetes. This study aims to develop the EIS technique so that it can be used to classify diabetes mellitus using machine learning with the backpropagation method. The data source was obtained from direct measurements in the laboratory using 90 mice (*Mus musculus*) that were made to suffer from diabetes mellitus. Mice were confirmed to have diabetes mellitus through a fasting blood sugar test (FBST) as a reference, then their cell electrical properties were measured using EIS. The measurement data will be made into a dataset for a machine learning model with the backpropagation training method consisting of input layers, hidden layers, and output layers. Paired data parameters used as input and output layers are frequency, phase, and impedance with blood glucose levels. The results of making a machine learning model to develop the EIS technique in classifying diabetes mellitus produced a fairly good performance index with an accuracy of 98.39 %, precision of 99 %, recall of 97 %, F1-score of 98 %, and specificity of 99 %. EIS development with the help of machine learning that utilizes the backpropagation method can be used to classify diabetes mellitus. The results of developing EIS using machine learning can be used to classify diabetes mellitus independently in a short time but have high accuracy.

**Keywords:** Backpropagation, Classification, Diabetes mellitus, Electrical impedance spectroscopy, Machine learning

## Introduction

Electrical Impedance Spectroscopy (EIS) is a technique that has been widely used to study the electrical properties of various materials, including biological tissues [1]. This method works by measuring the electrical response of a material to a small electric current at various frequencies. The main advantages of EIS lie in its non-invasive, cost-effective, and relatively easy-to-implement nature, making it a potential tool for various medical applications, such as cancer detection, fat tissue analysis, and physiological condition

monitoring [2,3]. However, despite its promise, EIS has several limitations that need to be overcome. One of the main challenges is the complexity of the data generated, which is often difficult to interpret without in-depth analysis. In addition, the application of EIS in the diagnosis of certain diseases, including diabetes mellitus, is still underdeveloped, and existing research focuses more on the application of EIS for general tissue analysis. This gap opens up opportunities to explore

how EIS techniques can be utilized more specifically in the diagnosis of chronic diseases [4,5].

Diabetes mellitus has always been a serious and urgent challenge to global health. The International Diabetes Federation (IDF) states that the prevalence of diabetes mellitus has increased significantly in the last 5 years. This reflects a worrying trend worldwide. According to data from IDF, in 2021, there were 537 million cases of diabetes mellitus, and it is projected to increase to more than 700 million cases by 2045 [6,7]. Diabetes mellitus can affect the quality of life of sufferers and contribute greatly to high morbidity and mortality in society. In an effort to face challenges that occur, the development of diabetes mellitus diagnostic methods continues to be developed to be able to detect diabetes earlier and preventive measures can be taken earlier. Conventional methods used to detect diabetes mellitus are random blood sugar tests (RBST), fasting blood sugar tests (FBST), oral glucose tolerance tests (OGTT), to hemoglobin A1c (HbA1c) [8-10]. Conventional methods sometimes make patients uncomfortable, time-consuming, prone to fluctuations, and have special protocols such as fasting and anhydrous glucose consumption. Other methods that have been developed include hyperinsulinemic-euglycemic clamp, glucose-insulin ratio (G/I ratio), homeostatic model assessment (HOMA), and quantitative insulin sensitivity check index (QUICKI). Some of these methods have better accuracy than conventional methods but are still relatively expensive and not affordable for everyone [11-13].

Recently, a screening method for diabetes mellitus based on the electrical properties of cells using the Electrical Impedance Spectroscopy (EIS) technique has been proposed. In previous studies, the EIS technique was only used to identify cell and tissue damage but was not yet able to classify a disease such as diabetes [14]. Electrical Impedance Spectroscopy (EIS) has the advantages of being easier to implement, cheap, safe, real-time and does not produce radiation. Several previous studies have shown that EIS can be used to evaluate the occurrence of cardiac dysfunction, breast cancer diagnosis, blood cell deformation analysis due to storage, cell damage studies due to indoor pollutants, food quality testing, and plant characterization [15-17]. Although EIS has many advantages, it also has several disadvantages. Namely it tends to display impedance

information with a lot of complex data, so it requires an expert in the field to read, analyze, and associate the EIS output results with the disease suffered [18].

EIS techniques have not yet been able to independently classify diabetes mellitus because no studies have specifically analyzed impedance characteristic patterns in diabetes [19,20]. Addressing this issue requires integrating EIS techniques with artificial intelligence approaches, such as machine learning, to process complex data output from EIS into meaningful, automatically classifiable information. A study by Pessoa *et al.* [21] on the use of Electrical Impedance Tomography (EIT) integrated with machine learning was able to differentiate between healthy and unhealthy lung conditions with 66 % accuracy. Although accuracy was relatively low, the study demonstrated promising potential. Furthermore, findings from Chen *et al.* (2024) confirmed that the EIS approach supported by machine learning can overcome conventional diagnosis limitations in identifying vulnerable atherosclerotic plaques. The lesion plaque classification results showed a very high accuracy of 92.59 % [22]. A review of recent studies over the past 5 years shows a research gap in diabetes disease classification based on impedance. Therefore, this study aims to fill that gap. This research is not only built on theoretical assumptions but is also based on a clear scientific need and global trends in the development of intelligent medical diagnostic technologies [23-25].

This research novelty lies in the EIS method integration with the backpropagation algorithm to classify diabetes mellitus based on blood impedance patterns. This is a new approach that has not been extensively explored in previous literature, which mostly focused on the use of EIS for general detection without specific classification of diabetes. This study contributes to the development of an intelligent and sustainable diagnostic system capable of automatically, precisely, and efficiently interpreting impedance data. The key points that make this paper worth writing are (1) Early diagnosis urgency of diabetes mellitus, (2) Currently used conventional diagnostic methods limitations, (3) EIS's great potential as a non-invasive diagnostic method that has not been widely explored for diabetes classification, and (4) Machine learning application as an effective solution to address the complexity of EIS data. This combination creates a new

system that can assist medical professionals in providing faster and more accurate diagnoses [26,27].

The machine learning method used in this study is backpropagation because it has a simpler architecture, a high level of flexibility, and scalability compared to other methods. Backpropagation is able to solve various

learning problems ranging from classification to regression. Several previous studies have shown that backpropagation is very effective in training models with thousands of parameters, exploring complex features on large datasets, and has high prediction accuracy, as shown in **Table 1**.

**Table 1** Accuracy of previous research findings using backpropagation algorithm.

Sample case	Author	Year	Accuracy	Source
Early prediction of cardiac tumors based on cardiac mass classification in echocardiogram images using backpropagation artificial neural networks.	Annamalai and Muthiah	2022	98.85 %	[28]
Diagnosis of dental caries in digital radiography using backpropagation neural networks.	Geetha <i>et al.</i>	2020	97.1 %	[29]
Potential use of feed-forward back propagation neural networks for lung cancer detection.	Nanglia <i>et al.</i>	2021	98.08 %	[30]
Fruit classification based on visual features using backpropagation neural networks.	Ghazal <i>et al.</i>	2021	100 %	[31]
Credit card fraud detection using artificial neural networks and backpropagation.	Dubey <i>et al.</i>	2020	99.96 %	[32]
Comparison of chronic kidney disease prediction using random forest and back propagation neural network algorithms.	Snegha <i>et al.</i>	2020	98.40 %	[33]

The challenges of using the backpropagation method are the selection of network architecture design, hyperparameter tuning, training data quality, and the risk of overfitting [34]. These challenges can actually be solved by adding optimization techniques such as Adam optimizer, batch normalization, and root mean square propagation to obtain good performance and efficiency [35,36]. This study aims to develop an EIS technique with a backpropagation method in classifying diabetes mellitus. Based on all the latest literature studies in the development of diabetes mellitus diagnostic technology, we want to provide a comprehensive view of the backpropagation method used in developing sustainable EIS in the future. This study is expected to provide new contributions related to the progress of medical tomography and diabetes mellitus diagnosis in helping patients and doctors obtain guidance, recommendations, and medical decisions.

## Materials and methods

### Experimental animal treatment

This study obtained data sets from direct experiments in the laboratory using 90 mice (*Mus*

*musculus*) weighing  $29 \pm 0.7$  g. The mice used were male, with an age of 3 months permitted by the ethics committee of Brawijaya University. The mice were randomly divided into 6 groups, 15 mice for each group. The mice were then acclimatized for 7 days in a cage environment with a controlled room temperature of  $25 \pm 2$  °C (humidity of  $48 \pm 8$  %, with a 12-hour dark/light cycle) at Biophysics Laboratory, Brawijaya University. After acclimatization phase, mice received streptozotocin injection for seven days at a dose of 10 (Group-1), 15 (Group-2), 20 (Group-3), 25 (Group-4) and 30 mg/kgWB (Group-5). The selection of low-dose STZ injections was intended to mimic type 2 diabetes pathophysiology commonly observed in humans, characterized by insulin resistance followed by progressive  $\beta$ -cell dysfunction. The Streptozotocin injection route used was the intraperitoneal (IP) method, which was carried out once a day. The control group did not receive streptozotocin injection and was only given food and drink from starch (same diet as the other groups) [37].

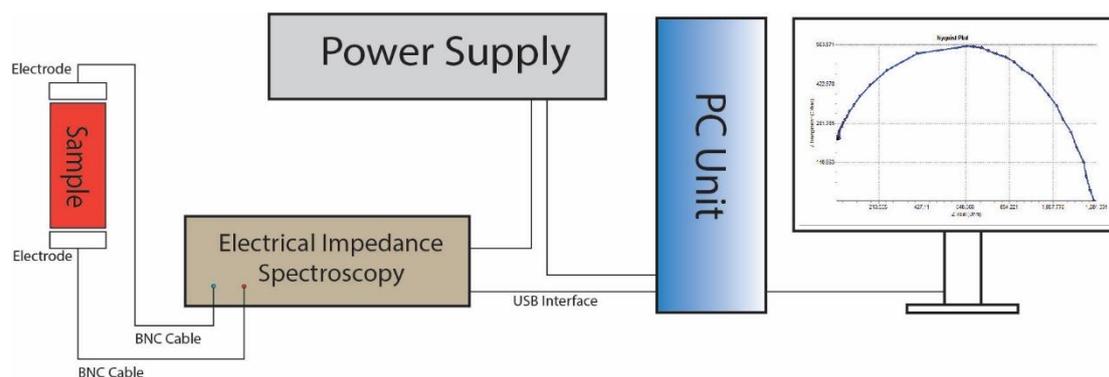
### Measurement of blood sugar levels

All mice had their blood sugar levels measured periodically using the fasting blood sugar test (FBST) method. Blood sugar levels were measured once a day using a calibrated glucometer (Accu-Check Active Roche diagnostic), which has an accuracy of  $\geq 95\%$  after the mice had fasted for 12 h to check for diabetes mellitus. Mice were considered pre-diabetic if their blood sugar levels were between 140 and 199 mg/dL and diabetic if their blood sugar levels exceeded 200 mg/dL [38]. If diabetes is known, the next step is to measure the electrical impedance value using Electrical Impedance Spectroscopy (EIS).

### Electrical impedance spectroscopy (EIS) measurement design

EIS system is designed to measure electrical impedance at various frequencies using a current of 10

microamperes. EIS unit is equipped with parallel plates as measuring electrodes connected via bayonet naur connector (BNC) cables, as shown in **Figure 1**. Applied current frequency ranges from 100 to 100,000 Hz to capture the electrical response of mice blood samples. Blood sampling is done through the tail vein. Mice tail is first dipped in warm water ( $\pm 40^\circ\text{C}$ ) to expand the vein. Mice's blood is then carefully taken using a lancet needle as much as 0.2 mL. The blood sample is then placed on the surface of the EIS electrode. Data processing is carried out automatically using EIS unit software so that impedance ( $Z$ ), phase, and frequency values are obtained which are ready to be analyzed in the next stage [3]. The entire process of treatment of experimental animals has received approval from the Local Ethics Committee of Brawijaya University, which approved this research (ethics approval number: 128-KEP-UB 2023, date: 21.08.2023).



**Figure 1** Electrical Impedance Spectroscopy (EIS) setup schematic.

Data preprocessing steps in this study involve several systematic steps to ensure input quality into artificial neural networks. First, complex impedance data obtained from EIS is converted into 2 main components, namely impedance magnitude signal and phase angle [39]. These components are considered important because they physiologically reflect resistive and reactive characteristics of blood samples, which can differ between healthy patients, pre-diabetes, and diabetes mellitus. Data with extreme or outlier values outside of 3 standard deviations from the mean are statistically eliminated to avoid distortion in model training. After that, min-max normalization is applied to ensure that all features are on a uniform scale (0 - 1), preventing larger numerical values from dominating network learning. The frequency feature is not explicitly

used as input because measurements are taken at a fixed frequency, which is assumed to be constant. Feature integration is done by constructing a multivariate input vector based on pairs  $(|Z|, \theta)$  from multiple frequencies. This feature selection is based on literature showing that both are most relevant in describing bioelectric changes in diabetic patients' biological tissue [40].

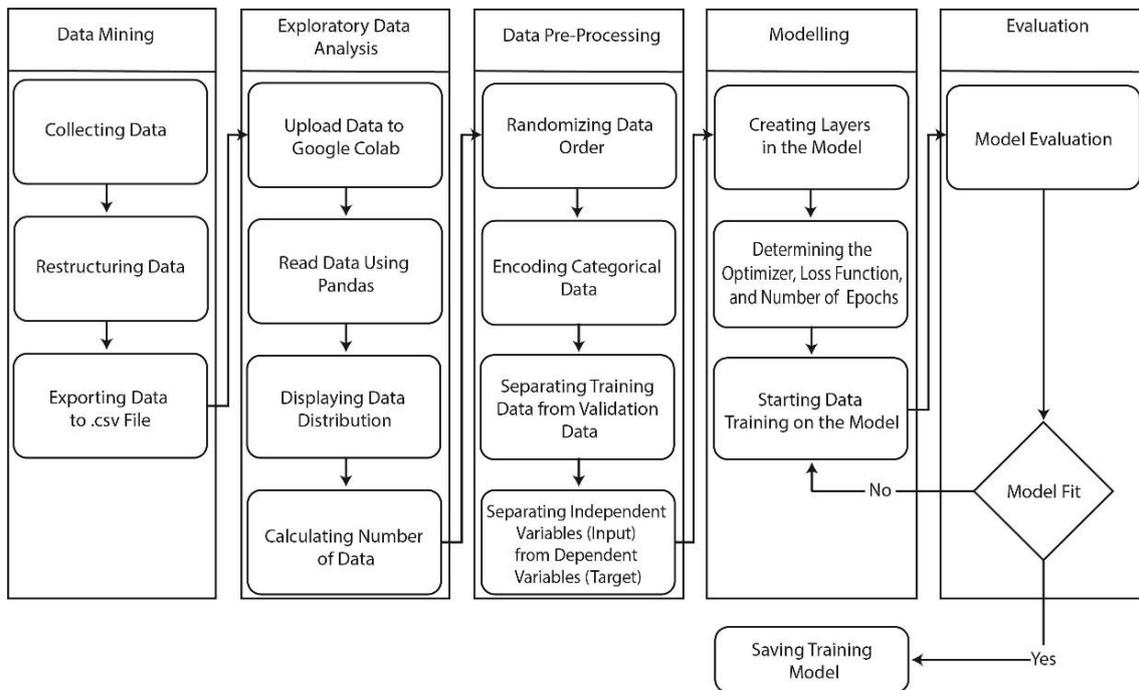
### Program flow chart

The machine learning program design in this study is included in the artificial neural networks (ANN) category. The program flowchart is shown in **Figure 2**. Implementation of artificial neural networks (ANN) was carried out to classify diabetes mellitus data using a multilayer perceptron (MLP) network consisting of an

input layer, a hidden layer, and an output layer. Each neuron processes data through the equation:

$$z_i = \sum_{j=1}^n w_{ij}x_j + b_i \quad (1)$$

$x_j$  is the input value,  $w_{ij}$  is the weight connecting neurons and  $b_i$  is the bias. The  $z_i$  The value obtained is then forwarded to a non-linear activation function, such as sigmoid, tanh, or ReLU, which functions to handle the limitations of linear models and capture complex relationships between variables.



**Figure 2** Flowchart for creating a diabetes mellitus classification program.

ANN training process is carried out through the backpropagation algorithm with the aim of minimizing the error between the output produced and the target value. The error is calculated using the Categorical Cross-Entropy loss function. The use of this loss function is crucial to measure how far the model prediction is from the expected value. Weight parameters are updated through the equation:

$$w_{ij}^{new} = w_{ij}^{old} - \eta \frac{\partial y}{\partial x_{ij}} \quad (2)$$

$\eta$  is the learning rate that determines how much adjustment is made.

This iterative process takes place over several epochs, where 1 epoch includes 1 full iteration through the entire training data. To improve performance and prevent overfitting, regularization techniques such as dropout are also applied. Dropout works by randomly

deactivating some neurons in the hidden layer during the training process so that the model is less dependent on certain neurons and can generalize better to new data. In addition, the selection of hyperparameters, such as the number of hidden layers, number of neurons in each layer, learning rate, and number of epochs, is done carefully through a cross-validation process to obtain an optimal combination of parameters. Hyperparameter tuning in this study was carried out systematically through a manual grid search approach. The range of hyperparameters tested includes learning rate, number of neurons, and number of epochs, as shown in **Table 2** [41].

We have made significant improvements to the machine learning method used. This study does not rely solely on the backpropagation old version but also integrates various modern algorithmic update techniques. We use Adam Optimizer as a weight update algorithm because of its efficiency in handling varying

gradients and accelerating convergence. In addition, batch normalization is applied to each hidden layer to reduce dependency on parameter initialization and speed up the training process. Regularization is enhanced through the use of adaptive dropout techniques to prevent overfitting in large networks. Network architecture is also improved through a gradual

fine-tuning and cross-validation approach, exploring neuron numbers and hidden layers to obtain an optimal configuration suited to impedance data complexity. With the combination of this method, the model developed has moved beyond machine learning’s old version and has been further enhanced by following current best practices in deep learning [42].

**Table 2** Backpropagation model hyperparameter tuning configuration.

No	Hyperparameter	Range of tested values	Best value	Reason
1.	Learning Rate	0.0001, 0.0005, 0.001, 0.005 and 0.01	0.001	Provides stable and fast convergence
2.	Number of Neurons (Hidden Layer)	16, 32, 64 and 128	64	The balance between accuracy and complexity
3.	Epoch	100, 200, 300, 400 and 500	400	Stable accuracy was achieved at the 400th epoch
4.	Optimizer	SGD, RMSProp and Adam Optimizer	Adam Optimizer	Best performance in accelerating convergence
5.	Activation Function (Hidden Layer)	Sigmoid and ReLU	ReLU	Prevents vanishing gradient, suitable for ReLU
6.	Activation Function (Output Layer)	Softmax and Sigmoid	Softmax	Suitable for multi-class classification
7.	Loss Function	MSE, Categorical Cross-Entropy	Categorical Cross-Entropy	Suitable for multi-class classification with 1-hot labels

**Evaluation model**

Parameters used to evaluate each model are accuracy (3), precision (4), recall (5), specificity (6), and F1-score (7). TP, TN, FP, and FN are true positive, true negative, false positive, and false negative values, respectively.

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

$$\text{Precision} = \frac{TP}{(TP + FP)} \tag{4}$$

$$\text{Sensitivity} = \frac{TP}{(TP + FN)} \tag{5}$$

$$\text{Spesificity} = \frac{TN}{(FP + TN)} \tag{6}$$

$$\text{F1 Score} = 2 \times \frac{(\text{Precision}) \times (\text{Recall})}{(\text{Precision} + \text{Recall})} \tag{7}$$

Accuracy evaluates the accuracy of the model and describes the ratio of impedance data number accurately

classified to the total number of impedance data tested. Model precision represents the ratio of impedance data accurately classified from the prediction of impedance data that have the same class. Recall or sensitivity represents the ratio of impedance data accurately classified as class one from a total number of impedance data predicted. Specificity is the truth of negative predictions compared to all negative data. At the same time, the F1-score states the average value of precision and recall. This value can be used for model optimization towards better precision or recall [43].

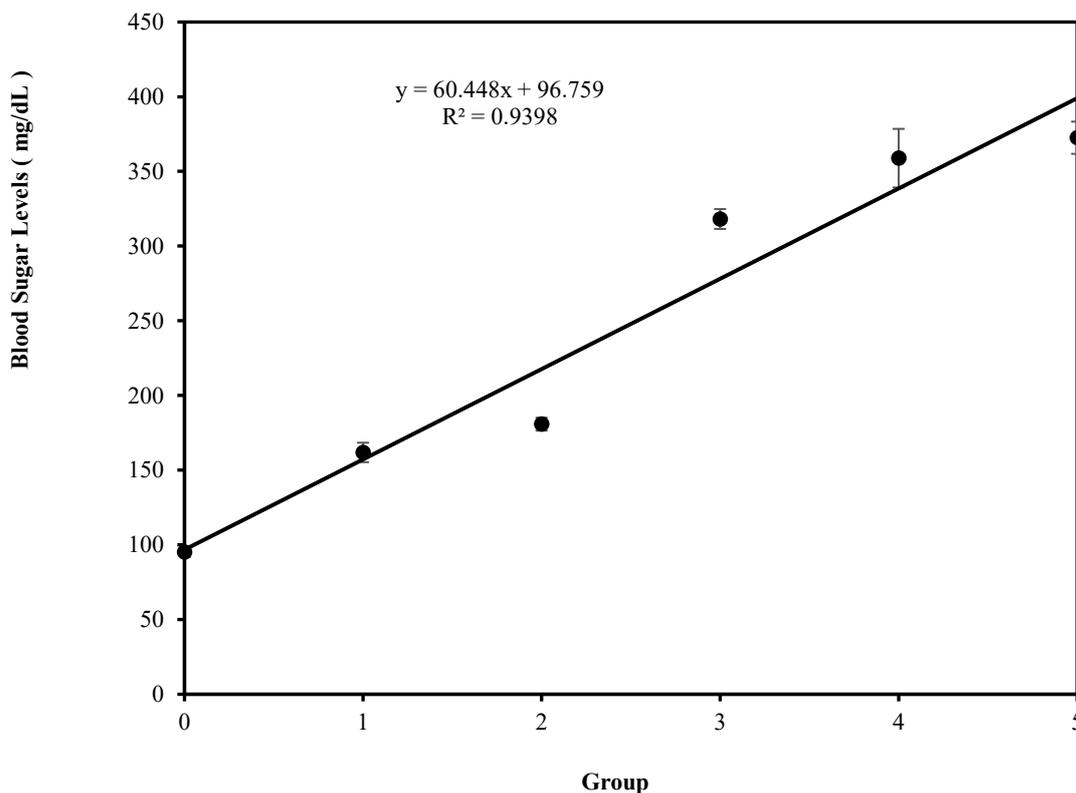
**Statistical analysis**

Analysis of variance (ANOVA) and Pearson correlation were used to assess the significance and differences between groups. Calculations were performed using Statistical Software 13.0 (10). ANOVA test with a *p*-value < 0.05 was assumed to indicate statistical significance. The correlation coefficient *r* = 1 indicates a perfect positive relationship, *r* = -1 indicates

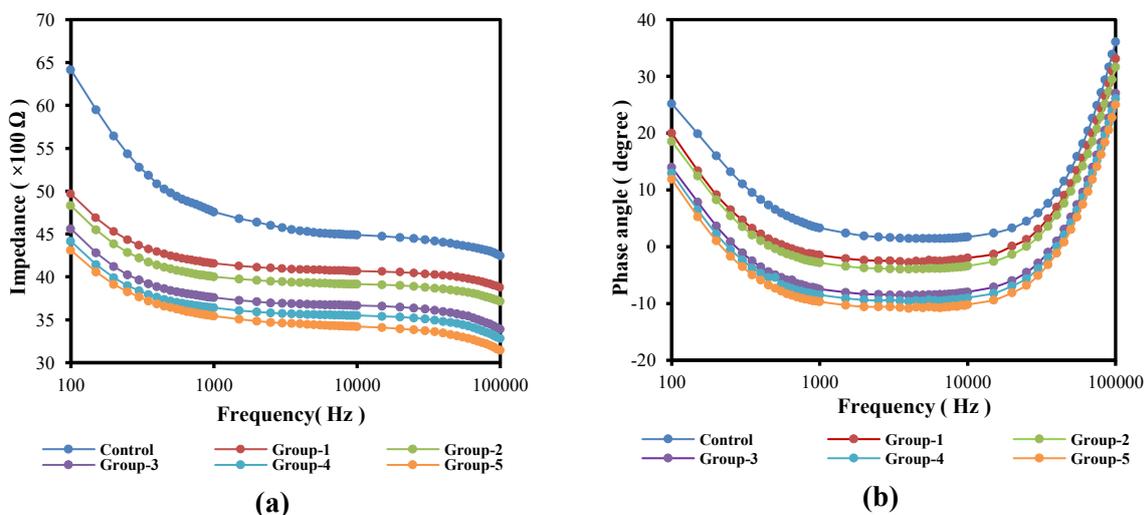
a perfect negative relationship, and  $r = 0$  indicates no linear relationship between 2 variables [44].

**Limitation**

This study uses murine data validation rather than direct human population validation. The study did not measure hydration status but focused on standard control measurements such as lighting, humidity, and availability of food and drinking water.



**Figure 3** Blood sugar levels of mice for each treatment.



**Figure 4** Frequency relationship graph against impedance value (a) and phase angle (b).

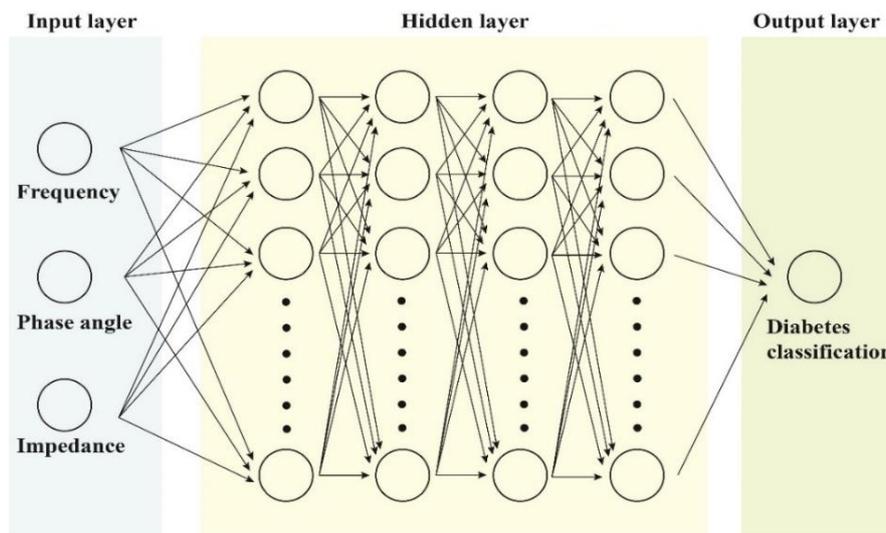


Figure 5 Illustration of architecture layers that have been built.

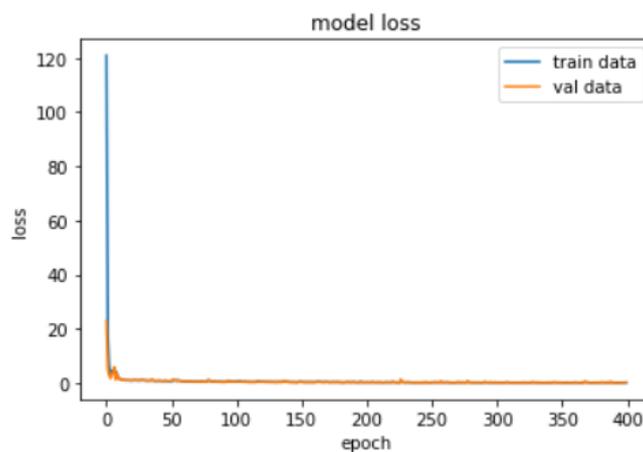


Figure 6 Loss curve depicting model prediction error.

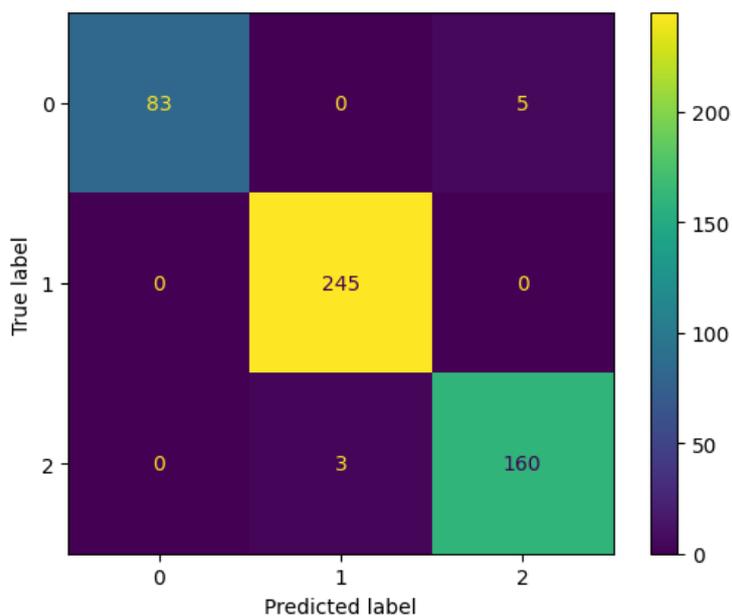


Figure 7 Confusion matrix of the backpropagation model.

## Results and discussion

### Results

Measurement results showed an increase in blood sugar levels for the streptozotocin injection group (**Figure 3**). Group-1 and Group-2 experienced an increase in blood sugar levels of 70.3 and 90.2 % when compared to the control group. Blood sugar levels of Group-1 and Group-2 tended to be closer but were much different from Group-3, Group-4, and Group-5.

Percentage increase in blood sugar levels of Group-3, Group-4 and Group-5 was 234.6, 277.5 and 291.9 %. This finding indicates that streptozotocin injection successfully caused mice to experience pre-diabetes (Group-1 and Group-2) and diabetes (Group-3, Group-4 and Group-5). Statistically, the increase in blood sugar levels and the dose of streptozotocin showed a significant difference with a  $p$ -value of 0.0008 and a correlation factor of  $r = 0.96$ . This proves that the relationship between the 2 is very strong, plus a very small standard deviation explains that data is relatively consistent.

Analysis of electrical impedance value and phase angle is shown in **Figure 4**. Measurement of electrical impedance and phase angle using the EIS technique shows well-organized data distribution between control, pre-diabetes (Group-1 and Group-2), and diabetes mellitus (Group-3, Group-4 and Group-5) groups. The control group showed the highest impedance value in the entire frequency range (100 Hz to 100 kHz), which reflects the electrical properties of healthier and optimal body tissues. In contrast, impedance values of pre-diabetes and diabetes mellitus groups were lower, with a more significant decrease in the diabetes group. In the phase angle graph, the control group also had the highest value at low to medium frequencies.

In contrast, the diabetes mellitus group showed consistently lower values in all frequency ranges. This difference provides an early indication of changes in the dielectric properties of body tissues due to metabolic influences, especially in pre-diabetes and diabetes mellitus conditions. The closeness of impedance and phase angle patterns between Group 1 and Group-2 (pre-diabetes group) is an interesting finding. At low to mid frequencies (100 Hz to 10 kHz) both groups show almost similar values, both in impedance and phase angle.

Electrical impedance value and phase angle phenomenon indicate that body tissue in the pre-diabetes stage is still in a relatively homogeneous condition. This homogeneity can be explained by the distribution of tissue fluid that has not shown significant changes even though there has been an initial metabolic disorder, such as insulin resistance or increased blood glucose levels [45]. The results of statistical analysis showed that impedance values between groups had significant differences, as shown in **Table 3**. This pattern indicates that tissue in the diabetes stage is more affected by physiological changes that cause an increase in phase angle when frequency increases. Significant positive relationship across groups reflects that changes in the phase angle can be used to distinguish clinical conditions clearly. The stronger nature of the relationship in pre-diabetes mellitus shows its potential as an early indicator of metabolic changes in body tissue [46,47].

Electrical Impedance Spectroscopy (EIS) measurement data is used to build a backpropagation training model consisting of 3 layers (input, hidden and output), as shown in **Figure 5**. Input and output layers are paired data parameters consisting of frequency, phase, and impedance values paired with the blood glucose levels of mice, as shown in **Table 4**. The hidden layer in this study is composed of 64 artificial neurons that have a collection of weighted inputs and procedures for producing output through activation functions. The type of hidden layer used in this study is a dense layer with a Rectified Linear Unit (ReLU) activation function, while the output layer uses a softmax activation function.

The results show that the ReLU activation function on the hidden layer and softmax on the output layer produce extraordinary capabilities in recognizing impedance patterns with a learning rate of 0.001 for the classification of healthy, pre-diabetic, and diabetic categories. Adam optimizer and categorical cross-entropy loss function are also applied to update network weights, thereby increasing training efficiency and computation time [48].

The accuracy curve graph in **Figure 6** shows an increasing trend in accuracy from the initial epoch to epoch 400, which reaches stability at a final value of around 96 %. This confirms the model's ability to

classify diabetes conditions well. At the same time, the loss curve shows a significant decrease with a final value approaching 0.1992, which indicates that prediction error has been successfully minimized. These results also provide an illustration that the designed architecture is simpler but effective in processing complex EIS data without overfitting [49].

The results of the model evaluation showed excellent performance with an accuracy value of 98.39 %, precision of 99 %, recall of 97 %, F1-score of 98 %, and specificity of 99 %. These results confirm that the backpropagation training method is effective for diabetes classification [50]. This analysis also confirms that a simpler design of an artificial neural network with

optimized parameters allows a machine learning-based EIS system to produce fast, accurate, and reliable classification to support the diagnosis of diabetes mellitus [51-53]. Confusion matrix analysis in **Figure 7** shows how the model performs more comprehensively. In the healthy category, 94.32 % of samples were correctly classified, while 5.68 % were misclassified as diabetes. There was no misclassification from healthy category analysis to pre-diabetes (0 %), which shows that the model is able to recognize characteristics of this category with a very high level of accuracy. In the pre-diabetes mellitus category, model performance showed very impressive results.

**Table 3** Statistical analysis of electrical impedance values for each group.

Group	Condition	Correlation factor (r)	p-value (ANOVA)	Interpretation
Control	Healthy	0.82	$1.24 \times 10^{-14}$	Strong positive correlation, phase increases with frequency
Group-1	Pre-diabetes	0.88	$9.81 \times 10^{-19}$	Stability of phase changes due to slight disturbances
Group-2	Pre-diabetes	0.88	$2.22 \times 10^{-18}$	Dielectric properties similar to Group-1
Group-3	Diabetes Mellitus	0.87	$7.47 \times 10^{-18}$	Increase in phase angle due to physiological changes
Group-4	Diabetes Mellitus	0.88	$1.49 \times 10^{-18}$	Increase in phase angle due to physiological changes
Group-5	Diabetes Mellitus	0.87	$2.48 \times 10^{-14}$	Strong correlation with physiological changes

**Table 4** Data pairs in creating a model.

Input			Output	
Frequency (Hz)	Impedance ( $\Omega$ )	Phase (degrees)	Blood sugar levels (mg/dL)	Category
100	6,300 - 6,400	24 - 25	110 - 140	Healthy
100	4,700 - 4,800	17 - 20	140 - 199	Pre-diabetes
100	4,200 - 4,300	11 - 12	> 200	Diabetes
150	5,940 - 5,950	19 - 20	110 - 140	Healthy
150	4,400 - 4,600	11 - 13	140 - 199	Pre-diabetes
150	4,000 - 4,100	5 - 6	> 200	Diabetes
⋮	⋮	⋮	⋮	⋮
100,000	4,230 - 4,260	35 - 36	110 - 140	Healthy
100,000	3,640 - 3,790	31 - 32	140 - 199	Pre-diabetes
100,000	2,950 - 3,338	24 - 25	> 200	Diabetes

All analyzed sample data were successfully classified correctly with an accuracy rate of 100 % without any false positive or false negative errors. This confirms the model's ability to accurately recognize pre-diabetes characteristic patterns, which are very important for early detection. This success is a major highlight because accurate pre-diabetes detection can be an early preventive intervention to prevent the development of diabetes mellitus. On the other hand, in the diabetes category, 98.16 % of samples were correctly classified, while 1.84 % were misclassified as pre-diabetes. This false negative error indicates that, in some cases, the model has difficulty distinguishing characteristics between pre-diabetes and diabetes, especially for data that is on the threshold of these 2 categories [54]. Most misclassifications are seen in the transition between healthy and diabetes categories, as well as between pre-diabetes and diabetes. This is most likely due to overlapping data characteristics, such as impedance or phase values that are at the category boundaries. Further analysis of data distribution in misclassified groups can provide additional insights to improve model sensitivity. Nevertheless, model specificity still has a value of 99 %, which indicates that the model is still able to recognize negative samples (healthy category) very well so that the negative results provided can be trusted. This ability is very relevant in large-scale clinical applications, where fast and accurate results are needed [55].

## Discussion

Impedance patterns identified in this study reflect physiological changes in body tissues due to metabolic disturbances associated with diabetes mellitus. The decrease in impedance values in the diabetes group compared to the control group indicates changes in fluid distribution and increased vascular resistance, which are hyperglycemia characteristics [3,5]. The lower phase angle in the diabetes group suggests a reduction in the membrane's capacity to store electric charge due to cell membrane dysfunction related to oxidative stress and chronic inflammation. Chronic hyperglycemia is known to cause glycosylation of proteins and lipids, which impacts the structure of the cell membrane and the dielectric properties of tissues. As a result, body tissues in diabetic conditions exhibit lower electrical

conductivity, as evidenced by the decrease in impedance values at high frequencies (1,000 Hz - 100 kHz). Changes in phase angle and impedance values in body tissues are closely related to physiological mechanisms affected by diabetes mellitus. Under normal conditions, the cell membrane functions as a dielectric component that regulates ion flow and maintains an electrical charge difference between intracellular and extracellular environments [56]. At low frequencies, electric current tends to flow around the cell membrane, while at high frequencies, current can penetrate the membrane, reflecting intracellular conditions. Chronic hyperglycemia in diabetes leads to membrane protein glycosylation and increased oxidative stress, which damages the lipid bilayer structure and alters the dielectric properties of the cell membrane. As a result, there is a decrease in membrane integrity and its ability to store electrical charges, reflected by the decrease in phase angle. Redistribution of body fluids due to changes in osmolarity and microvascular damage leads to a reduction in impedance values. In pre-diabetes, these changes begin to appear, although they are not yet as significant as in diabetes mellitus [57].

Clinical implications of false-positive results identified in confusion matrix analysis, amounting to 5.68 % misclassified as diabetes mellitus instead of being categorized as healthy, require special attention. In a clinical context, this can lead to patient anxiety. However, from an early detection perspective systems, false positives are generally more acceptable than false negatives. This is because patients still undergo further confirmatory diagnosis through laboratory tests before receiving diabetes mellitus treatment. Impedance range overlap between categories in **Table 4** indicates significant overlapping among healthy, pre-diabetes, and diabetes conditions. This phenomenon is common in bioimpedance-based measurements due to highly variable biological properties within the human body. Factors such as viscosity, intracellular and extracellular distribution fluids, electrolyte levels, and body temperature can influence measured impedance values [4,58]. Moreover, impedance values are not only affected by blood glucose levels but also by physiological conditions that are inherently individual. This reinforces the appropriateness of using artificial neural network methods with backpropagation

algorithms for impedance data analysis. Machine learning enables the modeling of non-linear relationships among multiple input parameters, such as frequency, impedance, and phase, allowing simultaneous and deeper capture of multivariable patterns. This approach does not merely consider a single value or range but also identifies the structural pattern of data distribution as a whole. Therefore, even though there is numerical overlap among categories, machine learning can distinguish latent features representing each class. This is evidenced by the model high accuracy, which compensates for inherent biological data variability within the human body [59].

The machine learning model with the backpropagation training method in this study showed very good performance in classifying impedance data into 3 categories (healthy, pre-diabetes and diabetes). Model evaluation results obtained showed the model's ability to recognize complex patterns from the Electrical Impedance Spectroscopy (EIS) dataset. A high level of specificity reflects the excellent ability of the machine learning model to minimize the occurrence of false negative classification errors [60]. Following is a

comparison of some machine learning performances in previous studies for the classification of diabetes mellitus. Performance comparison of the classification algorithm shown in **Table 5** shows that results of ANN machine learning model performance with backpropagation training provide better performance in the classification of diabetes mellitus compared to previous studies [22,43,61-63].

The backpropagation training method used in this study is able to provide significant advantages in terms of architectural simplicity, flexibility, and computational efficiency. This model has also been shown to overcome the main challenge of EIS, namely complex data analysis, but still produces high-performance metrics, far surpassing other approaches such as Support Vector Machine (SVM) or Random Forest, which generally require more complicated parameter tuning [64]. Compared with conventional diagnostic methods such as fasting blood sugar test (FBST) and hemoglobin A1c (HbA1c), a method developed in this study has important implications in the development of impedance data-based diagnostic technology [8-10].

**Table 5** Comparison of classification algorithm performance from various measurements.

Classification algorithms	Precision (%)	Recall (%)	F-score (%)	Accuracy (%)
Naive Bayes (NB)	75.9	76.3	76	76.3
Support Vector Machine (SVM)	42.4	65.1	51.3	65.1
Decision Tree	73.5	73.8	73.6	73.8
Logistic Regression	76.2	71.5	72.9	79.5
Random Forest	72.8	69.9	70.9	76.1
K-Nearest Neighbors (KNN)	71.1	69	69.7	74.8
Gradient Boosting Classifier	77.3	74.7	75.4	79.2
ResNet-7	100	67.8	80.8	83.3
DenseNet-9	80.9	100	89.4	92.5
ANN + Backpropagation	99	97	98	98.3

The simpler network architecture of the machine learning model that has been created also provides efficient computational time that can be adapted for standalone clinical devices [65]. Another uniqueness of this approach is the optimization applied, such as the Adam optimizer and the ReLU activation function that allows model training to take place efficiently even though the analyzed dataset is more complex [66]. In

clinical settings, this EIS-based system can be developed into a portable device that allows for continuous patient monitoring. This can support personalized approaches in diabetes management, enabling doctors to tailor disease interventions based on real-time data [67]. EIS techniques supported by machine learning also free patients from radiation risks, making it safe for repeated use, even in vulnerable

populations such as children or the elderly [68]. This finding opens up opportunities for diagnostic tool development, such as faster, more accurate, affordable, and non-invasive portable gadgets for a broader population, particularly in resource-limited areas [69,70]. The main challenges in realizing this device include the need for calibration against biological variability between individuals (e.g., hydration status and body temperature), as well as the need for further clinical validation in large populations. Portable device development must also involve longitudinal testing and supporting sensor integration to ensure reliable tools in various clinical contexts [71].

Electrical Impedance Spectroscopy (EIS) technique development supported by machine learning does offer an innovative approach to diabetes mellitus classification. Still, several challenges need to be solved, such as increasing the sensitivity of the model to data at the threshold between the pre-diabetes and diabetes categories [72]. Enriching the dataset with variations in impedance characteristics and phase angles at the beginning of training can help overcome this overlap [73]. Potential confounding factors such as hydration status may influence electrical impedance measurement results. Tissue impedance is affected by body water content since water is an excellent electricity conductor. Individuals experiencing dehydration will exhibit higher impedance values compared to normal conditions. Dehydration may affect model's accuracy in classifying blood glucose status. Conversely, hyperhydration may also artificially lower impedance values. Future studies are recommended to control hydration status before collecting impedance data or at least measure hydration levels to correlate them with impedance data. Adding this parameter could improve classification accuracy and reduce likelihood of errors caused by non-metabolic factors. This aligns with more robust development and reliable diagnostic system for clinical applications [74].

This study selected a machine learning model based on backpropagation (multilayer perceptron/MLP) for Electrical Impedance Spectroscopy (EIS) data classification, considering specific data characteristics and the intended application of this system in real-time portable diagnostic devices. EIS data we used consists of impedance values and phase angles at several frequency points, arranged in a fixed numerical vector form and lacking spatial structures like images

(commonly used in CNNs) or dynamic temporal sequences (more suitable for LSTM). Therefore, a feed-forward structure powered by a backpropagation algorithm is highly suitable for capturing discriminative patterns in this data [75]. The main advantage of this approach lies in its computational efficiency and low complexity, which are essential for integration into cloud-based systems or embedded devices with limited power and processing capacity. Furthermore, backpropagation models with simple architectures offer better interpretability, facilitate the tuning and debugging process during development, and accelerate training and inference phases. We acknowledge that deep learning approaches such as CNN or LSTM can offer additional benefits, especially in cases involving more complex or multivariate data. However, in the context of 1-dimensional EIS data, as used in this study, the backpropagation model has proven to be effective and efficient. For further development, we plan to conduct comparative studies with deep learning or hybrid models to evaluate potential performance improvements while considering trade-offs between accuracy, efficiency, and hardware requirements for real-world applications [76].

On the other hand, distribution analysis of classification errors in the confusion matrix can be a reference and provide additional insights to improve model accuracy. Optimization techniques such as Bayesian optimization are also relevant to optimizing hyperparameters, thereby increasing training efficiency. By continuing to take steps to improve, the developed system will be closer to the reliability required in clinical settings [77,78]. One of the limitations of this study is the use of a mice (*Mus musculus*) animal model that is induced with diabetes using streptozotocin (STZ). Although this model is widely used in diabetes research, there are several pathophysiological differences between this model and human diabetes. Induction with STZ causes direct damage to pancreatic beta cells through oxidative stress and lipid peroxidation, leading to a drastic decrease in insulin production. This resembles type 1 diabetes in humans, whereas most cases of human diabetes mellitus are type 2, characterized by insulin resistance accompanied by gradual insulin secretion dysfunction. STZ mice model also does not fully reflect metabolic complexity and genetic factors influencing the development of type 2

diabetes in humans, such as obesity, chronic inflammation, and adipose tissue dysfunction. Nevertheless, this model remains relevant for evaluating bioelectric changes in body tissues due to hyperglycemia, as hyperglycemia is a common factor found in all types of diabetes [79].

### Conclusions

This study successfully developed an Electrical Impedance Spectroscopy (EIS) technique combined with a backpropagation-based machine learning model for the classification of diabetes Mellitus. The constructed model demonstrated high performance with 98.39 % accuracy, 99 % precision, 97 % recall, 98 % F1-score, and 99 % specificity. These results indicate the model's capability to recognize impedance data patterns to differentiate between healthy, pre-diabetes, and diabetes categories accurately. EIS data analysis showed that the diabetic group experienced a significant decrease in impedance values and phase angles compared to the control group, indicating physiological changes in tissues due to metabolic disorders. Pre-diabetes group showed impedance and phase angle values that were close to each other, reflecting relatively homogeneous tissue conditions. These findings affirm EIS's potential for early detection of diabetes through changes in body tissue's electrical properties. The developed machine learning model features a simple yet efficient architecture, supported by the ReLU activation function and Adam optimizer, which enhance training speed and accuracy. The system was developed using a cloud-based platform that supports computational efficiency and potential integration into portable devices. Overall, this approach offers a fast, non-invasive, accurate, and independent alternative diagnostic method for diabetes detection and classification.

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### Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT to enhance the clarity of the writing. After using the ChatGPT, the authors reviewed and edited the content as needed and took full responsibility for the publication's content.

### CRedit Author Statement

**Muhammad Faisal:** Methodology, Supervision, Visualization, Validation, and Writing – original draft.

**Unggul Pundjung Juswono:** Conceptualization, Formal analysis, Investigation, and Validation.

**Didik Rahadi Santoso:** Funding acquisition, Data curation, and Validation.

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