

The Model Development for Forecasting the NS1Ag Antigen Examination Results of Dengue Fever Patients Using the Multi-Layer Perceptron Neural Network



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ABSTRACT

The objective of the article is to develop a model for forecasting the NS1Ag antigen examination results of dengue fever patients by using the Multi-Layer Perceptron Neural Network. The data used for developing the model was the results of the antigen type NS1Ag tests collected from a certain hospital's information system. The data dated from October 2018 – March 2020 with the number of 1,916 records. The data featured with 11 attributes. The Resample and SMOTE techniques were applied to adjust the imbalance of the data by increasing the size of data from 100% to 200%. The effectiveness evaluation results of the model using the percentage split of 70:30 revealed that the imbalance-adjusted model using the SMOTE method with the size of 200% and the Multi-Layer Perceptron Neural Network technique provided the accuracy of 93.54%. This provided higher accuracy compared to the model using the Multi-Layer Perceptron Neural Network solely. The results of the study show that the model could be used for forecasting the NS1Ag antigen examination results of dengue fever patients. It can be applied as a tool to support doctors and nurses to diagnose the dengue fever accurately and filter patient transfers to the laboratory appropriately.

Key words: Dengue Fever, Multi-Layer Perceptron Neural Network, Resample, SMOTE.

1. INTRODUCTION

Dengue fever is a severe disease that can kill patients in a short amount of time, causing public health problems in Thailand. The Ministry of Public Health identifies dengue fever as a severe disease that must be reported to the Bureau of Epidemiology under the Department of Disease Control; the investigation must be urgently operated within 24 hours. Annual statistics show the epidemic of dengue fever and its

death toll. According to the statistical reports of the epidemic and dead tolls conducted by the Bureau of Vector Borne Diseases, the Department of Disease Control, and the Ministry of Public Health, there were 71,976 dengue fever patients in 2018 with 103 deaths in Thailand, indicating the death rate of 0.13%. However, the number of dengue fever patients had increased by 1.5 times compared to the same period of the previous year [1]. The epidemic of dengue fever each year causes a high number of patients to be diagnosed in the hospital. The checklist of matters to be used for diagnosing dengue fever in a laboratory are as followed: (1) screening for the hematological changes by using the Complete Blood Count (CBC) test, which consists of the WBC count (white blood cell) test, the PLT count (blood platelet) test, and the HCT blood test based on the guideline for dengue fever diagnosis. Nevertheless, this preliminary examination is not only limited to dengue fever [2, 3], but it is available for low-cost examinations with the capital cost of 30-40 baht; (2) the diagnosis for dengue fever specifically, which is the immunology diagnosis by using examination kits based on the immunochromatography that can check antigens of the virus (Dengue NS1Ag) and antibodies (IgM, IgG). However, these examination kits have a higher cost of 200-400 baht, and the resources usage review from the Department of Clinical Pathology found out that the immunochromatography examination kits provided the positive results of 30% to 60% only. This reflects that the examination offered low specificity. Thus, identifying criteria for immunochromatography examinations using the number of white blood cells and blood platelets appropriate for the hospital services beforehand can increase time swiftness, specificity and effectiveness in diagnosing dengue fever. This also helps in cutting costs and budgets when buying examination kits.

Therefore, the research team decided to develop a model for forecasting the NS1Ag antigen examination results of dengue fever patients by using the Multi-Layer Perceptron Neural Network as an instrument to assist doctors and nurses to

diagnose dengue fever accurately. It can also be used as a tool for filtering patient transfers to the laboratory appropriately.

2. DENGUE HEMORRHAGIC FEVER

Dengue hemorrhagic fever is a disease caused by being infected by the Dengue virus that has *Aedes aegypti* (or common house mosquitos) as carriers. It is a common disease in tropical countries and usually spreads over the rainy season of each year. The symptoms of dengue fever vary from mild to fatal levels if not treated in time.

2.1 The Cause of The Disease

The cause of the disease is the spread of the Dengue virus with the *Aedes aegypti* as carriers. There are four types of Dengue viruses, including DENV-1, DENV-2, DENV-3, and DENV-4. Female house mosquitos are common carriers. When these house mosquitos bite the patients, the dengue virus will be embedded in the mosquitos' stomachs and salivary glands with the rest time of 8-12 days. Whenever the mosquitos bite other individuals, the virus would enter their bloodstreams and cause the epidemic of the disease [4].

2.2 Examination Methodology

The examination methodology for dengue fever is quite challenging due to the variety of symptoms. Thus, the accurate examination by using the clinical symptoms or using the symptomatic definitions is difficult. The most accurate method is to use laboratory examinations and physical check-ups [4].

A. Preliminary diagnoses

- The patients who have acute fever together with at least each of the two following symptoms; headache, sore eyes, muscle aches, joint pain, bone pain, and rash.
- The common hemorrhages are petechiae or nose bleed.
- Tourniquet tests which provide a positive predictive value of 63%, sensitivity of 98.7%, and specificity of 74-78%. Tourniquet tests provide positive results of about 50% on the first day, and then the positive results will increase to 80% and 90% on the second day and the third day, respectively.
- The clinical blood count (CBC) test shows the result of ordinal changes at the pre-entering and entering crisis stage of the disease, or when $WBC \leq 5,000$ cells/m³ with lymphocyte and atypical lymphocyte, and blood platelet $\leq 100,000$ cells/m³ with lower Neutrophil and 10-20% increased HCT.
- When there is evidence of the plasma leakage, such as having pleural effusion or ascites or high level of protein/low level of albumin in the blood.

B. The detection of DENV NS1 Antigen

DENV NS1 is a highly conserved glycoprotein that can be found in both membranes and the secretion of NS1Ag serum of the early-stage dengue fever patients. The NS1Ag is high in bloodstreams, so the application of the NS1 diagnosis is used for diagnosing the early stage of dengue virus infection before

the creation of IgM or IgG antibodies. The NS1 in the serum can be detected by using the ELISA examination or Lateral Flow Based Rapid Diagnosis Test (RDTs)/Immunochromatography produced by different companies with various speeds and specialties.

3. IMBALANCE DATA RESOLUTION

3.1 The Synthetic Minority Over-Sampling Technique

The Synthetic Minority Over-Sampling Technique (SMOTE) is applied to solve the problem of imbalanced data by synthesizing the data. The data set with low inputs are increased in size of inputs equivalent to the data set with a higher number of inputs. This can be done by randomizing one value and find the differences between the value and other values, and then choose the most similar one [5].

3.2 The Resample Technique

The Resample is one of the techniques used for adjusting the imbalance of data, which also affects the accuracy of the classification. This method of data randomization creates the subsamples randomized from the data set by replacement or noReplacement. However, the limitation of this method is that it may create an overfitting situation [6].

4. THE MULTI-LAYER PERCEPTRON NEURAL NETWORK

The Multi-Layer Perceptron Neural Network (MLP) has consisted of three layers: the input layer, hidden layer, and output layer. The hidden layer can be composed of more than one layer. The artificial neural network with the backpropagation learning functions has the learning principle in which the 'weight' is changed in order to obtain the most accurate values by using the backpropagation learning technique. The parameters that affect the simulation are the learning rate and the momentum value. Moreover, the activation function also affects the effectiveness of the network as well. The Multi-Layer Perceptron Neural Network [7] is illustrated in Figure 1.

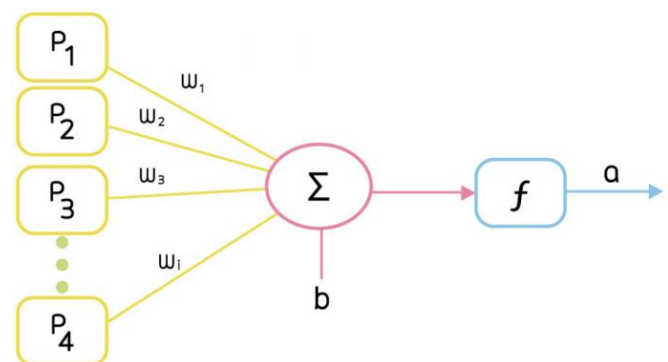


Figure 1: The Multi-Layer Perceptron Neural Network

Summation function in (1):

$$n = \sum_{i=1}^z x_i w_i + b(1)$$

Where

- n is the sum from the summation function,
- x_i is the value of i ,
- w_i is the weight of the neuron i ,
- z is the number of neurons in the input layer,
- b is the inclination value,
- i has the value of 1 to z .

The researchers of the forecast the dengue affirmed-patients using Artificial Neural Networks (ANNs). Raw data collected by the Singaporean National Environment Agency (NEA) was employed to develop a model of dengue patients' behavior based on the physical parameters, including average temperature, average relative humidity, and rainfall amounts. The findings revealed that the four key elements, including average temperature, average relative humidity, rainfall amounts, and the total number of dengue affirmed patients were highly effective for forecasting the number of dengue affirmed-patients. The ANNs are considered as highly productive processing systems for modeling and simulating the dengue affirmed-patient data evaluations. Aburas et al. (2010) [2]. To forecast the dengue affirmed-patients using the Artificial Neural Networks (ANNs). Raw data collected by the Singaporean National Environment Agency (NEA) was employed to develop a model of dengue patients' behavior based on the physical parameters, including average temperature, average relative humidity, and rainfall amounts. The findings revealed that the four key elements, including average temperature, average relative humidity, rainfall amounts, and the total number of dengue affirmed patients were highly effective for forecasting the number of dengue affirmed-patients. The ANNs are considered as highly productive processing systems for modeling and simulating the dengue affirmed-patient data evaluations. Pratiwi and Ariwibow (2012) [3]. In order to develop a dengue fever analysis, the severity of the disease is assessed on the basis of the value of eight-cell components in blood by using the Perceptron Artificial Neural Network method. The research process composes of three major steps, including laboratory data collection, data normalization with the Min-Max method, and dengue disease severity measurement toward the neural network. Employing the following parameters: learning rate equal to 0.3, tolerance value of 0.02, binary activation functioned with a threshold equal to 0.5, and 20 data sets as the number of training samples, the highest accuracy rate is given by system was 80%. Hence, it can be implied that the developed application system can be used for assisting doctors or other medical practitioners to assess the severity of dengue fever. Chaowanant et al. (2013) [8]. To develop a model forecasting the examination results of Cervical cancer patients towards the use of Multi-Layer Perceptron Neural Network.

The findings revealed that the Multi-Layer Perceptron Neural Network, adjusted by the SMOTE method and evaluated its

effectiveness by the 5-fold validation technique, provided the highest accuracy of 96.12% and sensitivity of 97.62%. Hambali and Akinyemi (2015) [9]. The study explored the prediction of master's degree students' performance by collecting 10 attributes and 108 registers of data about students. The imbalance of data was adjusted by employing the 100%-Random subsample resampling. Then, significant features were selected to formulate the model, which was later analyzed by the Multi-Layer Perceptron Neural Network, the RBF Neural Network, and Sequential Minimal Optimization.

The research results showed that the accuracy rate of adjusted-balance data towards the use of the Multi-Layer Perceptron Neural Network was 87.1287%, giving a better result than of non-adjusted data towards the use of the Multi-Layer Perceptron Neural Network (61.3861%). Vakili et al. (2015) [10]. To forecast the global solar radiation in Tehran regarding small-particle air pollution towards the use of artificial neural networks. The neural network modeling can be applied for forecasting the amount of solar radiation in a specific area. However, the estimated solar radiation data was not provided. Flores et al. (2017) [11]. To estimate the required amount of digoxin concentration for identifying cardio-activity of certain biophysical parameters in Tivela stultorum hearts towards the application of multi-layer perceptron artificial neural networks. The research findings revealed that the double-layer perceptron could be applied to gain the most accurate estimations of digoxin concentration needed in Tivela stultorum hearts by employing MLP-ANNs. AlAgha et al. (2018) [12]. The research team studied the classification of beta-thalassemia carriers among the Gaza Strip population in Palestine by using various data mining techniques. The examination results of red blood cells using Complete Blood Count were analyzed by which the researchers increased the size of the second data set from 100% to 500 % towards the application of the SMOTE technique. The findings showed that the Multi-Layer Perceptron Neural Network using the increased data set provided an accuracy of 99.73%, specificity of 99.82%, and sensitivity of 95.95%. Le et al. (2018) [13]. To predict bankruptcy of Korean case study companies towards the application of oversampling techniques. Oversampling techniques were applied to tackle the problems of financial dataset imbalance. The data was collected from Korean companies between 2016 and 2017. The findings indicated that oversampling techniques could enhance the effectiveness of the bankruptcy forecast model. Slimania et al. (2019) [14]. To estimate the amount of traffic in Morocco towards the application of artificial neural networks. The study made a comparison between the predicted traffic flow and the real dataset recorded on a section of a street as well as obtained from an acknowledged infrastructure manager in Morocco. The findings indicated that the most effective framework for this case study is the application of the Multi-Layer Perceptron Neural networks consisting of three hidden layers (5-8-2) by which the training set had an optimum total Mean Square Error of 0.00927 and the test set had an optimum total

Mean Square Error of 0.01321. Tamulionis and Serackis (2019) [15]. According to the prior research, it can be concluded that the Multi-Layer Perceptron Neural Networks have been applied in various fields, for example, disease diagnosis [2, 3, 8, 12], education [13], and traffic management [14, 15]. The results of the application of the Multi-Layer Perceptron Neural Networks in different areas led to the development of models established on this technique, which could be further used for effective data classification or data estimation. However, some studies figured out that the collected data was often imbalanced, which could lead to the lower effectiveness of the developed model. Therefore, some researchers proposed the data balancing technique [9, 12, 13]. In this research, the Resample and SMOTE techniques were applied to solve the problem of data imbalance in order to adjust the balance of data and then develop a balanced model. Balanced data contributes to the effectiveness of a model, providing better application and usage.

5. METHODOLOGY

The researchers conducted the research in four stages: 1) data collection, 2) the adjustment of imbalanced data using the Resample method and SMOTE method, 3) the model development using the Multi-Layer Perceptron Neural Network, and 4) the evaluation of the model's effectiveness as shown in Figure 2.

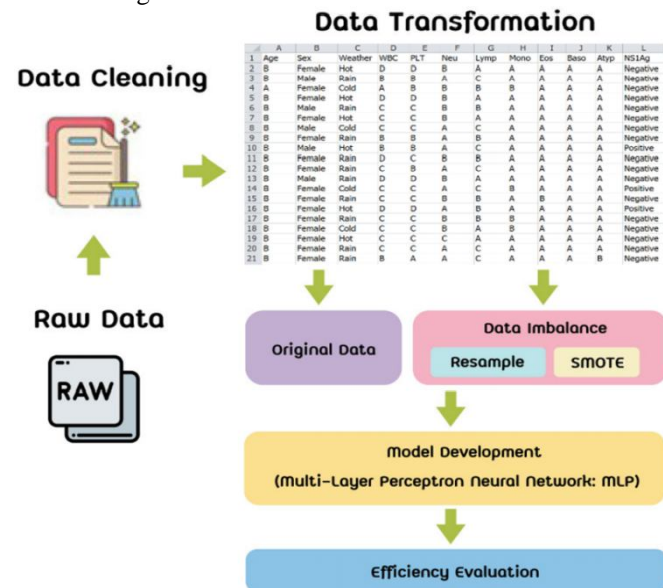


Figure 2: Conceptual framework

5.1 Data Collection

The data used in this study was the examination results of the NS1Ag antigen which had been collected from the information technology system of a hospital. The data had been collected from October 2018 to March 2020. The collected data of 8,331 records consisted of 11 attributes, including age, gender, examination month, the number of the white blood cells, the number of blood platelets, the number of the red blood cells, the HCT, neutrophils, lymphocytes,

monocytes, eosinophils, basophils, and atypical lymphocytes. After the data had been through the data cleaning process, the remaining data for this study was reduced to 1,916 records. Then, the data went through the data transformation process which was configured into the data in Table 1. The file was converted into a CSV file formatted for the operation in the Weka version 3.9 program as displayed in Figure 3.

	A	B	C	D	E	F	G	H	I	J	K	L
1	Age	Sex	Weather	WBC	PLT	Neu	Lymp	Mono	Eos	Baso	Atyp	NS1Ag
2	B	Female	Hot	D	D	B	A	A	A	A	A	Negative
3	B	Male	Rain	B	B	A	C	A	A	A	A	Negative
4	A	Female	Cold	A	B	B	A	B	A	A	A	Negative
5	B	Female	Hot	D	D	B	A	A	A	A	A	Negative
6	B	Male	Rain	C	C	B	B	A	A	A	A	Negative
7	B	Female	Hot	C	C	B	A	A	A	A	A	Negative
8	B	Male	Cold	C	C	A	C	A	A	A	A	Negative
9	B	Female	Rain	B	B	A	B	A	A	A	A	Negative
10	B	Male	Hot	B	B	A	C	A	A	A	A	Positive
11	B	Female	Rain	D	C	B	B	A	A	A	A	Negative
12	B	Female	Rain	C	B	A	C	A	A	A	A	Negative
13	B	Male	Rain	D	D	B	A	A	A	A	A	Negative
14	B	Female	Cold	C	C	A	C	B	A	A	A	Positive
15	B	Female	Rain	C	C	B	B	A	B	A	A	Negative
16	B	Female	Hot	D	D	A	B	A	A	A	A	Positive
17	B	Female	Rain	C	C	B	B	B	A	A	A	Negative
18	B	Female	Cold	C	C	B	A	B	A	A	A	Negative
19	B	Female	Hot	C	C	C	A	A	A	A	A	Negative
20	B	Female	Rain	C	C	A	C	A	A	A	A	Negative
21	B	Female	Rain	B	A	A	C	A	A	A	B	Negative

Figure 3: The data used for the model development

Table 1: The data attributes used for the development of the model forecasting the NS1Ag antigen examination results of dengue fever patients

No.	Features	Meaning	Feature variables
1	Age	Age	A: Age ≤ 2 B: Age > 2
2	Sex	Sex	Male: Male Female: Female
3	Weather	Weather	Hot: March, April, May, June Rain: July, August, September, October Cold: November, December, January, February
4	WBC	The number of white blood cells	A: WBC $< 3,000$ B: $3,000 \leq \text{WBC} \leq 3,999$ C: $4,000 \leq \text{WBC} \leq 10,000$ D: WBC $> 10,000$
5	PLT	The number of blood platelets	A: PLT $< 100,000$ B: $100,000 \leq \text{PLT} \leq 139,999$ C: $140,000 \leq \text{PLT} \leq 400,000$ D: PLT $> 400,000$
6	Neu	Neutrophils	A: Neu < 50 C: $50 \leq \text{Neu} \leq 75$ D: Neu > 75
7	Lymp	Lymphocytes	A: Lymp < 25 C: $25 \leq \text{Lymp} \leq 55$ D: Lymp > 55
8	Mono	Monocytes	A: Mono ≤ 10 B: Mono > 10
9	Eos	Eosinophils	A: Eos ≤ 5 B: Eos > 5
10	Baso	Basophiles	A: Baso ≤ 1 B: Baso > 1
11	Atyp	Atypical lymphocytes	A: Atyp = 0 B: Atyp > 0
12	NS1Ag	The result of the dengue virus (NS1Ag) examination	Negative: Negative result Positive: Positive result

5.2 Adjustment of The Imbalanced Data using The Resample and SMOTE Methods

After transforming the data, the researchers rechecked the accuracy of the data and found out that there were some groups of data with limited inputs. Therefore, the researchers adjusted the imbalanced data by using the Resample and SMOTE methods.

The adjustment of the imbalanced data by using the Resample method is applied whenever the forecasting results of a data set is imbalanced. It is done by configuring the randomseed equal to 5, configuring the noReplacement equal to False, configuring the biasToUniformClass equal to 0.0, and configuring the sampleSizePercent from 100% to 200%. According to the test results, the most suitable sample size of the data set for increasing the efficiency of the model is 200%. This means there are 3,832 records in total, doubling from the original records of 1,916.

The adjustment of the imbalanced data using the SMOTE method is operated by increasing the data set of the class that has a lower number of inputs. The configuration of the parameter is to increase the data by between 100% and 200%. According to the test results, the most suitable sample size of the data set for increasing the efficiency of the model is 200%. Hence, there are 5,106 records in total, which increased from the original number of records (3,190). The results of the data balancing with the Resample technique show Figure 4, with SMOTE shown in Figure 5 and by both methods are shown in Figure 6.

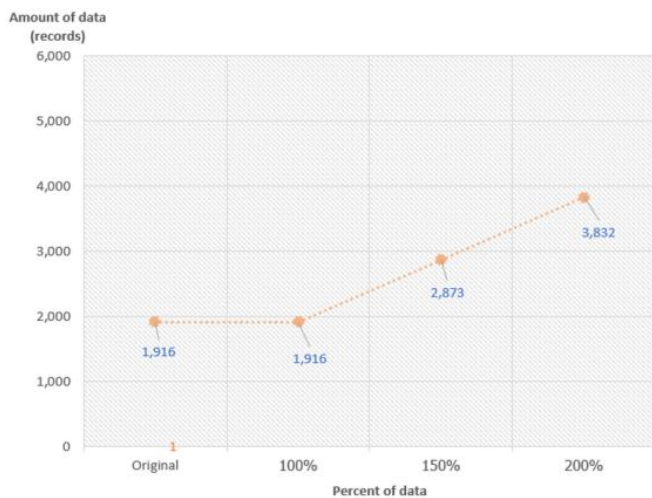


Figure 4: The adjustment of the data using the Resample method

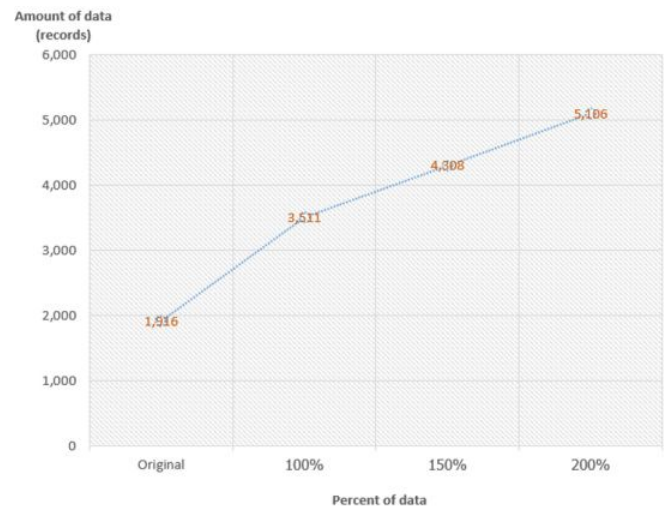


Figure 5: The adjustment of the data using the SMOTE method

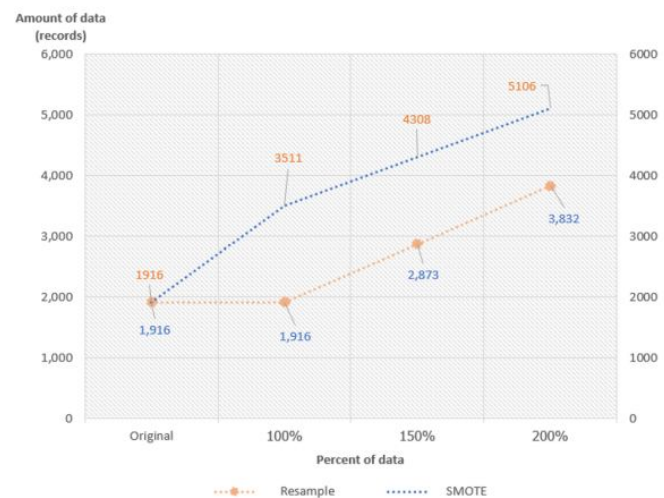


Figure 6: The adjustment of the data using the Resample and SMOTE methods

5.3 Model Development using The Multi-Layer Perceptron Neural Network

At this stage, the model for forecasting the NS1Ag antigen examination results of dengue fever patients were developed by using the Weka version 3.9 program. The configuration of the parameters are as follows: the learning rate is 0.3, the momentum is 0.2, the hidden layer is 5, and the training time is 500.

5.4 Model Evaluation

The model's effectiveness was evaluated by using the 70:30 percentage split method. The effectiveness of the model was evaluated by using the confusion matrix which is a method used for finding the accuracy of a classification model. This can be calculated by (2) [16–22], replacing the values shown in Figure 7.

	Predict : No	Predict : Yes
Actual : No	TN	FP
Actual : Yes	FN	TP

Figure 7: Confusion matrix

$$Accuracy = \frac{TP+TN}{TP+TN+FP+FN} \quad (2)$$

Where

TP refers to when the targeted class is 'Yes' and the model predicts it 'Yes,'

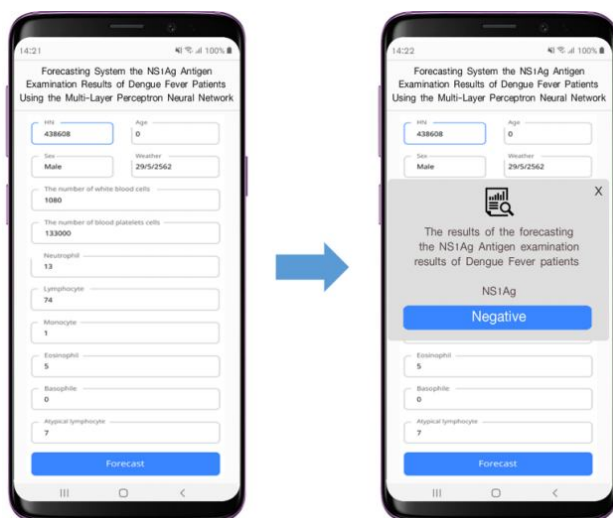
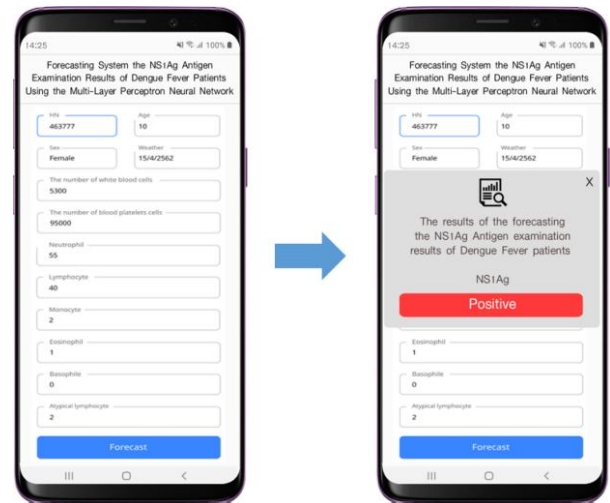
TN refers to when the targeted class is 'No' and the model predicts it 'No,'

FP refers to when the targeted class is 'No' but the model predicts it 'Yes,'

FN refers to when the targeted class is 'Yes' but the model predicts it 'No.'

5.5 Mobile Application Development

The developed model was applied to mobile application development. This application was developed in cross-platform to support both iOS and Android mobile devices. The application is combining the ionic framework, PHP, java programming for using the model and forecasting the NS1Ag antigen examination results of dengue fever patients. The screen design can be illustrated in Figure 8 and Figure 9.

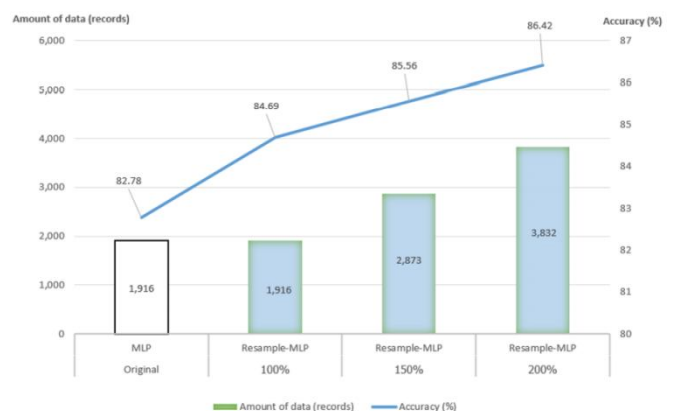
**Figure 8:** Screen design for forecasting the NS1Ag antigen on mobile application (negative result)**Figure 9:** Screen design for forecasting the NS1Ag antigen on mobile application (positive result)

6. RESEARCH RESULTS

The model's effectiveness was evaluated by using the 70:30 percentage split method. The model was developed by using the MLP method with some configurations as follows; the learning rate is 0.3, the momentum is 0.2, the hidden layer is 5, and the training time is 500. The evaluation results are illustrated in Table 2 and Figure 10 to Figure 12.

Table 2: The data attributes used for the development of the model forecasting the NS1Ag antigen examination results of dengue fever patients

Technique	Percent of data	Amount of data	Accuracy (%)
MLP	Original	1,916	82.78
Resample-MLP	100%	1,916	84.69
Resample-MLP	150%	2,873	85.56
Resample-MLP	200%	3,832	86.42
SMOTE-MLP	100%	3,511	90.12
SMOTE-MLP	150%	4,308	93.19
SMOTE-MLP	200%	5,106	93.54

**Figure 10:** The accuracy of the model using the Resample and MLP methods

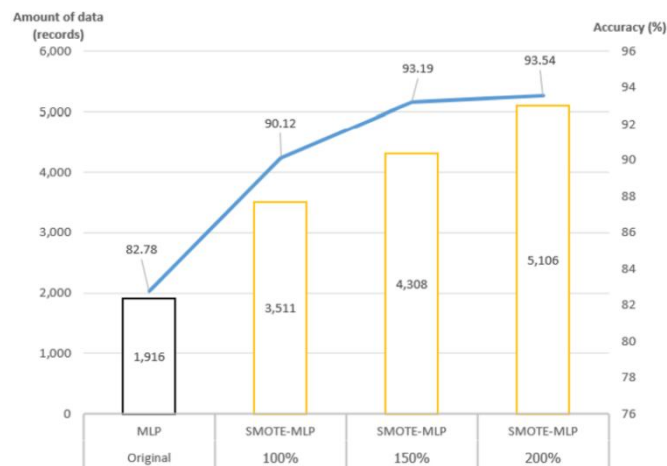


Figure 11: The accuracy of the model using the SMOTE and MLP methods



Figure 12: The comparison of the accuracy of the model using the Resample-MLP and SMOTE-MLP methods

7. CONCLUSION

This research aims to develop the model for forecasting the NS1Ag antigen examination results of dengue fever patients by using the Multi-Layer Perceptron Neural Network. The collected, imbalanced data had been adjusted by the application of the Resample and SMOTE methods. The study revealed that the adjustment of the imbalance using the SMOTE method by increasing the data size to 200% contributed to the most efficient model. After adjusting the imbalance, the data set was used for developing the model by using the Multi-Layer Perceptron Neural, and then was evaluated by using the 70:30 percentage split method. The results of the efficiency tests show that the model tested with the 70:30 percentage split method, adjusted (its imbalance) with the SMOTE method, and classified (the data) by the Multi-Layer Perceptron Neural Network produced the most efficient data classification. Its accuracy was 93.54% which was higher than the model using the Multi-Layer Perceptron Neural alone. These study results conformed to the study of Sato et al. (2013) [8] in that the application of the SMOTE method and the Multi-Layer Perceptron Neural Network

provided better classification than using the Multi-Layer Perceptron Neural solely.

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