SYSTEM IDENTIFICATION OF NONLINEAR AUTOREGRESSIVE MODELS IN MONITORING DENGUE INFECTION

[#]H. Abdul Rahim¹, F. Ibrahim² and M. N. Taib³

¹Department of Control and Instrumentation Engineering, Faculty of Electrical Engineering, Universiti Teknologi Malaysia, 81310 UTM Skudai, Johor, Malaysia.

²Department of Biomedical Engineering, Faculty of Engineering, University of Malaya, 50603 Kuala Lumpur, Malaysia.

³Faculty of Electrical Engineering, Universiti Teknologi Mara, 40450 Shah Alam, Selangor, Malaysia.

#Emails: herlina@fke.utm.my

Abstract-This paper proposes system identification on application of nonlinear AR (NAR) based on Artificial Neural Network (ANN) for monitor of dengue infections. In building the model, three selection criteria, i.e. the final prediction error (FPE), Akaike's Information Criteria (AIC), and Lipschitz number were used. Each of the models is divided into two approaches, which are unregularized approach and regularized approach. The findings indicate that NARMAX model with regularized approach yields better accuracy by 80.60%. The best parameters' settings for this thesis can be found using the Lipschitz number criterion for the model order selection with artificial neural network structure of 4 trained using the Levenberg Marquardt algorithm.

Index terms: dengue fever, NAR model, AIC, Lipschitz, FPE, ROC and AUC.

1. INTRODUCTION

Dengue fever (DF) ranks highly among the newly emerging infectious diseases in public health significance. Hence it is considered to be the most important of the arthropod-borne viral diseases. In Malaysia, the disease is endemic but major outbreaks seem to occur at least once in every four years [2]. Dengue fever was first reported in Malaysia after an epidemic in Penang in 1902 [3, 4]. Since the early 1970s, the World Health Organization (WHO) has been actively involved in developing and promoting strategies for treatment and control of dengue. In 1997, WHO published a second guide to the diagnosis, treatment and control of dengue haemorrhagic fever [1]. Dengue were reported throughout the year and started to increase from 1997 to 1998. In 1998, 27,373 dengue cases with 58 deaths were reported as compared to 19,544 cases with 50 deaths in 1997. This has shown an increase of 7,829 cases or 40.1% over the number of cases in 1997 [5]. Therefore, accurate classification of dengue infection a very useful tool for doctors in diagnosing diseases early.

Fatimah et. al. [6] describe a noninvasive prediction system for predicting the day of defervescence of fever in dengue patients using ANN. The developed system bases its prediction solely on clinical symptoms and signs and the results show that around 90% prediction accuracy.

This paper describes a noninvasive classification system for dengue infections using NAR models. The rest of the paper is structured as follows: In Section II nonlinear autoregressive (NAR) model is presented. Methods are provided in Section III. In Section IV shows the results. Finally, concluding remarks and discussions are presented in Section V.

II. NONLINEAR AUTOREGRESSIVE MODEL

The NAR model consists of an autoregressive which is represented as past output data and the nonlinear function was selected as hyperbolic tangent.

$$\hat{y}(t) = F[y(t-1), ..., y(t-n_y), u(t)]$$
(1)

where F is a nonlinear part, y(t) and u(t) represent the output and input, respectively. n_y is the associated maximum lags. Block diagram for NAR model is as shown in Figure 1.

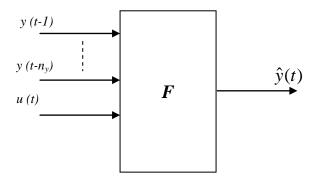


Figure 1: NAR Model

a. Model Order Selection

Model order selection is dependent upon the quality of the model since the model order is varied and the cost function is monitored. A useful measure to aid this procedure is to measure the significance of each additional model. Assessing the significance of each model is not only necessary for model order selection but also for further analysis of the estimated model and can aid the design and analysis of medical applications.

b. Model Estimation

The third step is model estimation, which involves determining the numerical values of the structural parameters, which minimise the error between the system to be identified, and its model.

c. Regularization

If the network has been trained to a very small value of criterion, the model needs not be particularly good. A good performance on the training set does not automatically imply that the model generalizes well to new inputs. In particular, it was shown that if the model structure was too large (contained many weights) it led to overfitting [15], that is, the noise in the training set was also modelled. The average generalization error was introduced as a quantity assessing a given model structure. One way of controlling the average generalization error was to extend the criterion with a term called regularization by simple weight decay [15]. The weight decay reduced the variance error at the expense of a higher bias error.

d. Model Validation

Receiver operating characteristic (ROC) curves are commonly used in medicine and healthcare [18], where they are used to quantify the accuracy of diagnostic tests [19, 20]. The performance of an "expert" human or machine, can be represented objectively by ROC curves [21]. Such curves show, for example, the trade-off between a diagnostic test correctly identifying diseased patients as diseased, rather than healthy, versus correctly identifying healthy patients as healthy, rather than diseased. Terms commonly used in ROC curves are sensitivity, specificity and diagnostic accuracy, to show the accuracy of the designed system.

i. Receiver Operating Characteristic (ROC) Curves

ROC curves display the relationship between sensitivity (true positive rate) and 1-specificity (false positive rate) across all possible threshold values that define the positivity of a disease. They show the full picture trade-off between true positive rate and false positive rate at different levels of positivity.

The ANN must be trained before the ROC curve can be generated. The resulting network is referred to as a "basic trained network". This initial instance of the ANN provides one operating point. The result is a set of instances of the network chosen to represent a point on the ROC curve. The goodness of this set of network instances are then evaluated using separate test data.

Table 1 shows a diagnostic accuracy results after training the ANN. The decision variable can produce two sets of values, which represents two category types dengue infection. The true dengue infection is denoted as D+, whereas the false dengue infection is indicated as D-.

Diagnosis (Dengue Infection) Test Positive Result Negative Total (Decision Model) (Dengue) (Healthy) TP Positive FP T+Т-Negative FN TNTotal D-D+

Table 1: Diagnostic Accuracy table

In general, four possible decisions and two types of errors are made when comparing a test result with a diagnosis, as shown in Table 1. If both diagnosis and test are positive, it is called a true positive (TP). The probability of the TP to occur is estimated by counting the true positives in the sample and dividing by the sample size. If the diagnosis is positive and the test is negative it is called a false negative (FN). False positive (FP) and true negative (TN) are defined similarly. The two sets of values produced in the threshold are the total positive and negative indicated as T+ and T-.

Sensitivity and specificity are the basic measures of the accuracy of the diagnostic test. They describe the abilities of the test to enable one to correctly diagnose disease when the disease is actually present and to correctly rule out disease when it is truly absent.

The accuracy of a test is measured by comparing the results of the test to the true disease status of the patient. Sensitivity and specificity depend on the threshold (also known as 'operating point' or 'cut point') used to define positive and negative test results. As the threshold level decreases, the sensitivity increases while the specificity decreases, and vice versa.

Sensitivity is the ratio or percentage of a probability that a test result will be positive when the diagnosis is present, also known as true positive rate (TPR), defined as:

$$Sensitivity: TPR = \frac{TP}{D+} \tag{2}$$

Specificity is the ratio or percentage of a probability that a test result will be negative when the disease is not present and also known as true negative rate (TNR), defined as:

$$Specificity: TNR = \frac{TN}{D-} \tag{3}$$

III. METHODOLOGY

a. Data Collection

The data were obtained from the previous work [22]. For the first group, the severity of the DHF is classified into grade I to IV, according to WHO recommendation [23]. Acute dengue infection was confirmed subsequently by the use of ELISA to detect elevated dengue specific IgM (primary infection) and IgG (secondary infection) [24]. Patient serum samples were tested for hemoglobin determination using an automated counter

(Coulter STKS machine). The second group is the control group for healthy female and male subjects.

The second group of patients (control subjects) who do not have past medical history of dengue were recruited and studied using the same guidelines as in the BIA subject preparation used for the first group [22]. The BIA safety measurements procedure and other safety precautions were made known to the subjects and their informed consent was obtained from each subject prior to the BIA measurement.

For the control subject, the weight was taken once. However for subjects with dengue infection, the weight was measured daily until upon discharged.

b. Clinical Experiments

One of the clinical methods in making dengue diagnosis is to establish the clinical history-taking, physical examination and investigation. Each patient undergoes detailed history taking, physical examinations and blood investigations following their admission. Clinical evaluations and haematological investigations are conducted continuously until they are discharged.

The patients were also admitted at different stages of their illness, thus it is important to have the results of clinical signs and symptoms, blood investigations, and other analyses dated with a consistent and proper reference point [22]. Nevertheless, thorough documentation of symptoms and blood investigations do not offer definitive advantage in the management and monitoring of dengue cases. A more useful measure is to develop a complete day-to-day profile of clinical manifestations and blood investigations made according to a proper reference point based on the 'Fever day' definition [22]. This is to ensure that the data used in the analysis will refer to a common reference point, regardless of how many days of fever the patient has experienced

The Hb status of control subjects cannot be determined at a low frequency of 50 kHz, since the membranes of blood cells will act as insulators. In DHF patients however, pathophysiological changes caused by the dengue infection lead to a plasma leakage. And this in turn causes low thrombocytopenia and coagulopathy [23]. It is therefore possible to estimate the Hb volume indirectly using the BIA technique.

c. BIA Experiments

The bioelectrical impedance experiments are conducted using the bioimpedance analyzer. It is important to note that there is no historical or clinical evidence that bioimpedance testing is unsafe, even for pregnant women or persons with pre-existing heart conditions. During the years 2001 and 2002, two hundred and ten adult patients aged twelve years old and above, with serological confirmation (WHO 1997) of acute dengue infection, admitted in HUKM, Malaysia were prospectively studied. At present, the knowledge acquisition to present pattern to classify the dengue infections is limited to the clinical symptoms and signs. Thus, only clinical symptoms were used as the input data for classify the dengue infections.

A total of one hundred and forty two volunteers with no past medical history were recruited and studied as the control subjects. For the control subject the weight was taken once, however for subjects with dengue infection the weight was measured daily until upon discharged.

The statistical analysis was performed using SPSS statistical package version 10.01 for Window 1998. Simple linear regression was used in the preliminary analysis for testing the significance of the variables. These variables were then included in the multivariate analysis. Multiple linear regression was used to analyse the control effects of the patient demographic and symptom variables and BIA parameters on Hb. The model was constructed in three steps as follows:

- a. When correlation exits between variables, one or more variables were excluded for the multivariate analysis.
- b. The demographic variables were first included in the model. Once the demographic predictors were identified, add in the BIA parameters and find, which of these parameters were important predictors.
- c. The last step was to include symptom and find out whether with the addition of this predictor will make further significant contribution or not.

The last step was to include symptom and find out whether with the addition of this predictor will make further significant contribution or not.

Only five variables are highly significant which gender, weight, reactance (Xc), vomiting and day of fever [22, 25-27].

These predictors will be the inputs for linear and nonlinear system identification based on ANN. All the inputs data for these models were normalized from '0' to '1'. Only for linear and nonlinear system identification based on ANN the output data were categorize into 2 parts, for classifying the dengue infections disease which is 0 for no dengue infection, while 1 for dengue infections.

Then, the input data were divided randomly, between 2 sets: a training set and a testing set. These five input variables were fed into the FFNN and trained using LM algorithm. During this process, the NAR application was optimized via four steps where each of these steps was implemented to find optimum value for the model order, the number of hidden layers, maximum iterations, and lastly the number of parameters regularization. At each experiment, the respective parameter to be optimized was varied while the other three were fixed. Selection of the optimum parameter value for each step was based on the performance evaluation of the model through the final prediction error (FPE) analysis as well as the diagnostic accuracy (DA). For simplicity, threshold for the output logic levels was fixed to 0.5 for each models used in this work. At the next stage, the most appropriate threshold level would be decided by analyzing the minimum *Euclidean Distance* (ED) values from the receiver operating characteristic (ROC) plot.

Finally, the area under the ROC curve was applied to measure the accuracy of dengue hemoglobin status in the diagnostic test.

d. Experiment for NAR Model

These experiments were designed to give better accuracy than the previous experiments (linear model). These experiments processes (data preprocessing, model design, model estimation and model validation) are described in next section.

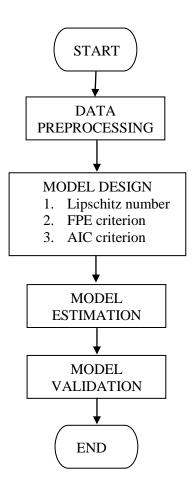


Figure 2: Nonlinear Model Development Process for NAR Experiment

i. Data Preprocessing

Two matrices were generated from the data collection: training, and test set. These data were then divided randomly into two sets: a training set, and a testing set to ensure that it generalizes well. All data were normalized so that that the dataset has zeroed mean and uniform standard deviation.

The training data was used to guide MLP weight updates during training. The test set was used to test the performance of the MLP.

ii. Model Design for Nonlinear Model

For nonlinear models, NAR, was used to monitor the progression of dengue infection based on hemoglobin. Input variables were fed into the feedforward ANN and trained using Levenberg-Marquardt algorithm. The number of hidden layers was set to be between 1 to 10 units. The number was chosen so as to reduce time consumption in training the data, and network overfitting [15]. A

transfer function for neurons in the hidden layers is hyperbolic tangent sigmoid and the single neuron in the output layer has a linear transfer function.

There were two approaches considered in this study, unregularized and regularized approach. Unregularized approach is the normal method used for training the networks, which is associated with Equation 3.42 for FPE. For the regularized approach, it was shown that one way of controlling the average generalization error was to extend the criterion with a term called regularization by simple weight decay. The weight decay reduced the variance error at the expense of a higher bias error. Nørgaard [15] showed that the value was obtained on validation data set when regularized approach was used. Figure 3 illustrates this approach.

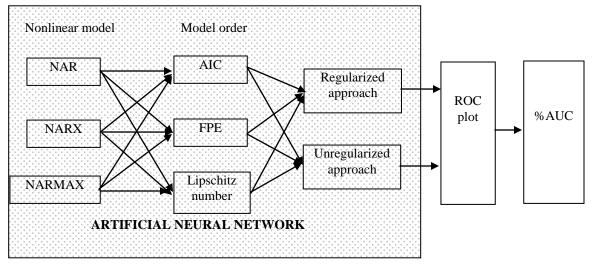


Figure 3: Steps to monitor progression of dengue infection based on hemoglobin using linear model

i. Model Estimation

The MLP application was optimized via four steps, each of which was implemented to find the optimum value for the number of neurons in the hidden layer, training iterations and regularization parameters. In each step, the parameter to be optimized is varied, while the other two are fixed. Selection of the optimum parameter value for each step was based on the performance of the model through the FPE analysis as well as DA. For simplicity, threshold for the

output logic levels was fixed to 0.5 for each model used in this initial work. The best model for the experiment was then selected for the final application.

ii. Validation of Nonlinear Models

In this stage, the most appropriate threshold level was decided by analyzing the minimum ED values from the ROC plot. Finally the AUC was applied to measure the accuracy of dengue hemoglobin status in diagnostic test.

IV. RESULTS

a. Dengue Data

During the year 2001 to 2002, two hundred and ten adult patients aged 12 to 83 years old, suspected of DF and DHF admitted to the Universiti Kebangsaan Malaysia Hospital (HUKM), were monitored. The dengue infection was also confirmed serologically by detection of IgM antibody using the ELISA method. For all the 210 dengue patients studied, 119 (56.7%) were male and 91 (43.3%) were females.

The sample size of the female was more than the male for DF by 4 patients. However, for DHF I the males exceeded the females by 11; the males increased by 22 compared to females in DHF II and there was only one female DSS patient. In the age distribution, the majority were mainly in the 15-24 years group age (35.71%), followed by the 25-34 years group age (25.24%). Those aged between 35-44 years constituted 20% for all cases. This indicates that the majority of the patients were teenagers and young adults, whom were more likely to be involved in outdoor activities and thus more likely to be exposed to the danger of dengue infection.

b. Bioelectrical Impedance Analysis

In the analysis of bioelectrical tissue conductivity (BETC) parameters for the healthy subjects, it was found that body capacitance (BC) and phase angle (α) were lower in the female subjects compared to their male counterparts (Table 5.2). On the other hand, resistor (R) and reactance (X_c) were higher in females than in males. A similar trend for the BETC parameters was also observed in dengue patients, where a higher α and BC values were found in males, and a higher R and X_c values were found in females. For example, on 'Fever day 0', the mean α for male was $6.69\pm0.91^{\circ}$ and female was

5.45±1.02°, while the mean BC was 821.24±187.58pF and 516.82±112.93pF for males and females, respectively. However, the female R (592.14±93.90 Ω) and X_c (56.92±15.73 Ω) were higher than the male R (462.77±76.81 Ω) and X_c (54.02±11.15 Ω), respectively (Table 2).

Table 2: BETC parameters for both control data and dengue patients

	MALE			
	Mean±SD			
Fever of Days	Phase Angle Body Capacitance		Resistor	Reactance
	(°)	(pF)	(Ω)	(Ω)
0	6.69±0.91	821.24±187.58	462.77±76.81	54.02±11.15
+ 1	6.70±0.88	819.61±170.48	462.31±73.31	54.34±11.62
+ 2	6.67±0.80	789.44±186.81	475.19±79.02	55.38±10.43
+ 3	6.75±0.82	785.81±189.71	481.26±82.81	56.82±11.39
Control data	7.35±0.76	818.08±158.03	504.03±63.44	74.57±70.79
	FEMALE			
	Mean±SD			
Fever of Days	Phase Angle	Body Capacitance	Resistor	Reactance
	(°)	(pF)	(Ω)	(Ω)
0	5.45±1.02	516.82±112.93	592.14±93.90	56.92±15.73
+ 1	5.38±0.83	523.39±107.77	574.39±95.24	54.31±12.75
+ 2	5.37±0.85	525.70±113.63	577.16±102.15	54.26±13.02
+ 3	5.43±0.99	527.83±125.93	582.74±116.07	55.48±15.69
Control data	6.31±0.63	556.90±101.18	634.69±71.55	69.86±8.44

c. Control Data

The healthy control data, a total of 144 volunteers with no past medical history were analyzed. The patients were between the ages of 13 to 60 years old, and 53 (37%) were males and 91 (63%) were females. The racial and gender distributions are shown in Figures 5.7 and 5.8. The majority of the confirmed patients were Malays (95 or 66.0%), followed by Chinese with 36 patients (25.0%), Indian with 3 (2.0%) and others with 10 (7.0%).

In the age distribution, the majority were mainly in the 15-24 years group age (35.71%), followed by the 25-34 years group age (25.24%). Those aged between 35-44 years constituted 20% for all races.

e. Experiment for Statistical Analysis

Correlations between variables were analyzed using Spearman's correlation coefficient. It is a standardized measure of the strength of the relationship between two variables that does not rely on the assumptions of a parametric test. A matrix is displayed giving the correlation coefficient between the two variables such as gender and height (0.647), underneath is the significant values of the coefficient (0.000) and finally the sample size (210). The significant value for this correlation coefficient is less than 0.05. Therefore, it can be concluded that there is a significant relationship between the gender and height. Linear regression was used to identify the most significant variable among the bioelectrical impedance analysis parameters. The significant variables were resistance and reactance (p<0.05). Table 5.3 shows the model parameters. This model includes nine variables predicting the Hb, but only four variables are highly significant.

Table 3: Significant parameters for 210 dengue patients on day-of-admission.

Coefficients (a)

Model	Unstandardized		Standardized		
	Coefficients		Coefficients		
	В	Standard Error	Beta	t	Significance
(Constant)	6.012	3.75		1.603	0.112
GENDER	1.309	0.551	0.338	2.373	0.02
RISK	-0.241	0.32	-0.063	-0.753	0.453
HEIGHT	0.020	0.025	0.096	0.82	0.414
RACE	0.066	0.177	0.031	0.375	0.709
WEIGHT	0.029	0.014	0.264	2.059	0.042
RESISTANCE	-0.002	0.004	-0.105	-0.514	0.609
REACTANCE	0.047	0.019	0.327	2.48	0.015
VOMITING	1.178	0.493	0.191	2.388	0.019
ANOREXIA	0.156	0.341	0.035	0.458	0.648

a. Dependent Variable: Hemoglobin

The best model produced by the multilinear regression using four variables (gender, weight, reactance and vomiting) only yields an accuracy of 43%. This model can be written as follows:

$$Hb = 6.012 + 1.309(gender) + 0.029(weight) + 0.047(reactance) + 0.19(vomiting) + \varepsilon$$
 (19)

where,

gender = 0 for female and 1 for male

weight =weight of patients in kg

react. = reactance of patients in ohm

vomiting = 1 for sign of vomit and 0 for no sign of vomit,

 $\varepsilon = \text{error term}$

f. AR Experiment

Three types of input variables, which consisted of a list of dengue clinical symptoms, physiological and BIA parameters, were used in the AR Experiments. These input variables were analysed and evaluated using SPSS based on the hemoglobin concentration.

g. Data Preprocessing

210 patients were monitored over a period of 4 succeeding days, depending on their severity and duration of stay in the hospital. The patients' symptoms, BIA parameters and physiological data were monitored daily to form a unique set of samples, and producing a total of 781 samples. All data were normalized from '0' to '1'. These data were then divided randomly into two sets: a training set consisting of 527 samples, and a testing set of 254 samples. Each case was arranged as column vectors in the datasets.

The results show that there were only one symptom (vomiting), two physiological data (gender and weight) and one BIA parameter (reactance) which were significant based on Experiment for SPSS. These predictors were subsequently used as inputs for Experiment for NAR. 'Fever day 0' to 'Fever day +3' were important references for the physiological changes in the clinical symptoms. All of these parameters were employed as the inputs for the system identification experiments.

h. Model Design

The model order was chosen using the Lipschitz number, FPE and AIC order selection criteria. Figure 4 illustrate Lipschitz number plots for five input variables (vomiting, gender, weight, day of fever and reactance) of dengue patients.

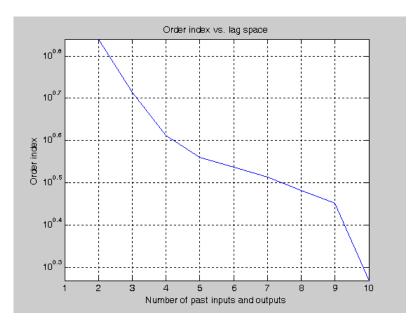


Figure 4: Model order of Lipschitz number criterion via AR model

From Figure 4, the optimal number of regression as the knee point of the curve was 4, so that the value of the model order was n_a =4.

i. Model Estimation

Figure 5 shows the Lipshitz number criterion for finding the neuron number in hidden layer. It can be seen that the DA line shows increasing trend at 3 neurons. Increasing the neurons after this did not improve the model effectiveness in recognizing the test data set despite the increasing trend of FPE. Thus, the network model that was iterated for 2 neurons and showed maximum accuracy (83.52%) is selected with the least value of error (0.071).

NAR MODEL Model order selection: Lipschitz Number Criteria (Maximum Iteration=300, stopping criterion=1x10-5, regularization value(D)=0)

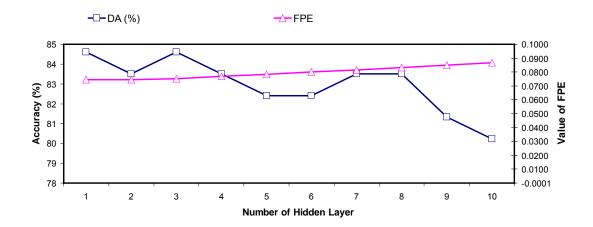


Figure 5: Plot of diagnostic accuracy and FPE against the number of neurons in the hidden layer using Lipschitz number criteria via NAR model

The iteration is also based on the highest DA and the least value of error. Figure 6 illustrates the model performance for finding the best iteration and the DA reached its maximum (91.21%) when 500 iterations were used, using Lipschitz number criterion.

NAR MODEL Model order selection: Lipschitz Number Criteria (Hidden Layer=3, stopping criterion=1x10-5, regularization value(D)=0)

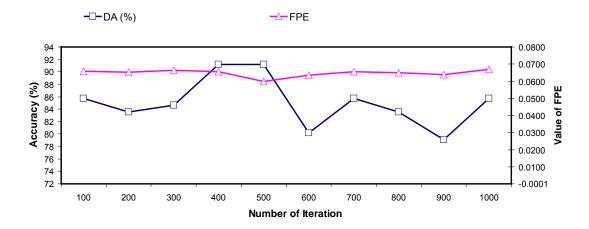


Figure 6: Plot of diagnostic accuracy and FPE against the number of iterations using Lipschitz number criteria via NAR model

These three steps are usually used for unregularized method. An addition of an extra step is necessary to find the best regularization parameters. The best regularization parameter selected was 0.0001 because the DA is 85.71% (reasonably high) and the value of the FPE was 0.064 (the least), hence meeting the maximum iteration (500) as shown in Figure 7.

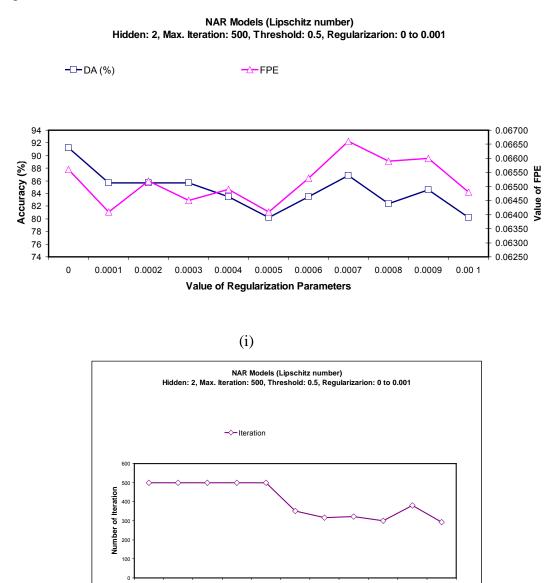


Figure 7: (i) Plot of diagnostic accuracy and FPE against the value of regularization parameters using Lipschitz number criteria via NAR model, ii) Plot of number of

(ii)

Value of Regularization Parameter

iteration against the value of regularization parameters using Lipschitz number criteria via NAR model

Table 4 tabulates the summary of the parameters of NAR model for the different types of model order criteria.

Table 4: NAR model with the different number model order criteria

Parameter	Lipschitz	FPE	AIC
Model order	4	15	25
Hidden Layer	2	4	4
Maximum	500	500	500
Iteration			
Regularization	1x10 ⁻³	$3x10^{-3}$	2x10 ⁻³

j. Model Validation for NAR Experiment

In general, Table 5 shows the different number of the model order using different types of criteria and the AUC performance. From this table, it was found that the Lipschitz number criterion for regularized approach produced the highest accuracy (80.60%) for the NAR model.

Table 5: A comparison of NAR models with the different number model order criteria for unregularized and regularized AUC performance.

Criterion	Model	AUC (%)	AUC (%)
	order	unregularized	regularized
Lipschitz	4	76.2	80.6
FPE	15	66.0	68.4
AIC	25	63.6	67.6

The model order, as given by the Lipschitz number criterion, was tested using Neural Network-based AR model. The overall performance of NAR model diagnosis is as shown in Table 6.

Table 6: The parameters of the diagnostic test using NAR model with different approaches.

	Criterion		
	Lipschitz	FPE	AIC
Unregularized			
Sensitivity	87.14	86.57	86.67
Specificity	85.71	83.33	80.00
Diagnostic Accuracy	86.81	85.88	85.33
Euclidean Distance	0.19	0.21	0.15
from point (0,1)			
Regularized			
Sensitivity	87.14	83.61	88.33
Specificity	80.95	83.33	86.67
Diagnostic Accuracy	85.71	83.54	88.00
Euclidean Distance	0.23	0.23	0.18
from point (0,1)			

For Lipschitz number criterion, the diagnostic accuracy of 86.81% was achieved for the unregularized method, whereas a small proportion of diagnostic error 13.19% has been observed for the total test group of 210 subjects. An 87.14% sensitivity, 85.71% specificity and 95.31% of positive prediction were evaluated for the designed model structure. The area under the ROC curve (AUC) was 76.2%. The regularized method illustrates 85.71% of accuracy in diagnosis while 14.29% is the indicated diagnostic error. Overall, the designed model structure has 87.14% sensitivity, 80.95% specificity and the positive prediction was 93.84%. The performances were measured based on the receiver operating characteristic (ROC) curves.

The overall performance of NARX model with unregularized approach is as shown in Table 6. The area under the ROC curve (AUC) was 76.20% is shown in Figure 8 (Lipschitz number). The closest ED is depicted from the ideal point (0,1) as 0.19 when the optimized model has a threshold of 0.4.

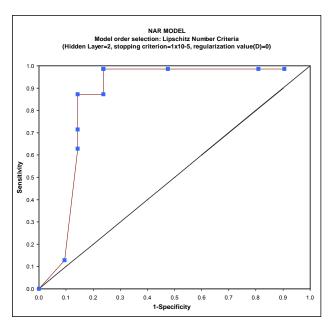


Figure 8: ROC curve for Lipschitz number criterion using NAR unregularized model

The ROC curve for the Lipschitz number criterion with regularized approach is shown in Figure 9. The total AUC can be derived by combining the individual area with respect to the labeled thresholds in the figure. For Lipschitz number criterion, AUC is 80.6%. The closest ED is depicted from the ideal point (0,1) as 0.23 when the optimized model has a threshold of 0.4.

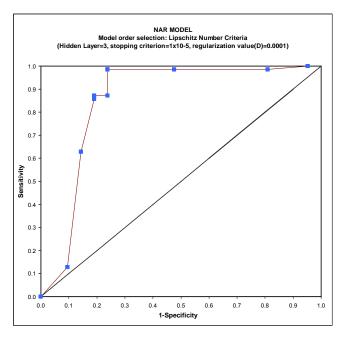


Figure 9: ROC curve for Lipschitz number criterion using NAR regularized model.

V. CONCLUSIONS

Using SPSS analysis, it was found that the work presented has successfully modeled heamoglobin status using selected physiological parameters (i.e. gender, vomiting, weight and day of fever) and BIA parameters (i.e. reactance).

The best model produced by the multilinear regression using four variables (gender, weight, reactance and vomiting) only yields an accuracy of 43%. This model can be written as follows:

 $Hb = 6.012 + 1.309(gender) + 0.029(weight) + 0.047(react.) + 0.19(vomiting) + \varepsilon$

NAR model has produced AUC of 72.60% using Lipschitz number with unregularized method but the AUC was improve by using the regularized method (80.60%)

The model accuracies in predicting the haemoglobin status, to indicate the dengue progressions, ranges from 43% (using the multilinear regression) to 80.60% (using NAR model).

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References

- [1] W. H. Organization, *Dengue Haemorrhagic fever Diagnosis, treatment, Prevention, and control*, 2nd ed. Geneva: WHO, 1997.
- [2] U.G. Kyle, I. Bosaeus, A.D. De Lorenzo, P. Deurenberg, M. Elia, J.M. Gomez, B.L. Heitmann, L. Kent-Smith, J. Melchior, M. Pirlich, H. Scharfetter, A.M.W.J. Schols and C. Pichard, "Biolectrical impedance analysis part1:review of principles and methods," *Clinical Nutrition*, vol. 23, pp. 1226-1243, 2004.
- [3] F. M. Skae, "Dengue fever in Penang," *Br. Med. J*, vol. 2, pp. 1581-1582, 1902.
- [4] S. C. Gordon, "Dengue: an introduction. In: Rudnick A, Lim TW, Eds. Dengue Fever Studies in Malaysia Institute for Medical Research Malaysia" *Bulletion*, vol. 23, pp. 1-5, 1986.

- [5] W. C. a. R. Annual Report, "Dengue Haemorrhagic Fever," Dept. of Medical Microbiology, Fac. of Medicine, University of Malaya, 50603 Kuala Lumpur Malaysia, 1998.
- [6] F. Ibrahim, M.N. Taib, W.A.B. Wan Abas, C.C. Guan, and S. Sulaiman, "A novel dengue fever (DF) and dengue haemorrhagic fever (DHF) analysis using artificial neural network," *Compu. Methods Programs Biomed.*, vol. 79, pp. 273-281, 2005.
- [7] P.M. Djuric, and S.M. Kay, "Order selection of autoregressive models," *IEEE Trans. On sig. Processing* vol. 40, no.11, pp. 2829-2833, 1992.
- [8] G.E.P Box, and J.M. Jenkins, "Time series analysis, forecating and control," *San Francisco:Holden Day*, 1970.
- [9] H. Akaike, "A new look at the statistical model identification," *IEEE Trans. On Automat. Contr.*, vol. 19, pp. 716-723, 1974.
- [10] J. Rissanen, "Modeling by shortest data description," *Automatica*, vol. 14, pp. 465-478, 1978.
- [11] R. L. Kashyap, "Optimal choice of AR and MA parts in autoregressive moving average models " *IEEE Trans. Patt. Anal. Machine Intelligent*, vol. 14, pp. 99-104, 1982.
- [12] G. Schwarz, "Estimating the dimension of the model," *Ann. Stat.*, vol. 6, pp. 461-464, 1978.
- [13] K.S. Narenda, and K. Parthasarathy "Identification and control of dynamical systems using neural networks," *IEEE Trans. On Nueral Networks*, vol. 1, pp. 4-27, 1990.
- [14] X. He, and H. Asada, "A new method for identifying orders of input-output models for nonlinear dynamic systems," *Proc. of the American Control* pp. 2520-2523, 1993.
- [15] M. Norgaard, "Neural network based on system identification toolbox," *Technical Report*, 00-E-891, *Department of Automation, Technical University of Denmark*, 2000.
- [16] A. Raganathan, "The Levenberg-Marquardt Algorithm," Georgia Institute of Technology, unpublished.
- [17] S. Roweis, "Levenberg-Marquardt Optimization," Univ. of Toronto, unpublished.

- [18] K.P. Adlassnig, and W. Scheithauer, "Performance evaluation of medical expert systems using ROC curves," *Compt. Biomed. Res.*, vol. 22, pp. 297-313, 1989.
- [19] J.A. Hanley, and B.J. McNeil, "The meaning and use of the area under a receiver operating characteristic (ROC) curve," *Radiology*, vol. 143, pp. 29-36, 1982.
- [20] T.J. Downey, D.J. Meyer, R.M. Price, and E.L. Spitznagel "Using the receiver operating characteristics to asses the performance of neural calssifiers," pp. 3642-3646, 1999.
- [21] B.J. McNeil, and J.A. Hanley, "Statistical approaches to the analysis of receiver operating characteristic (ROC) curves," *Medical Decision Making*, vol. 4, pp. 1984, 1984.
- [22] F. Ibrahim, "Prognosis of dengue fever and dengue haemorrhagic fever using bioelectrical impedance," PhD Thesis, Department of Biomedical Engineering, University of Malaya, July, 2005.
- [23] Dengue Haemorrhagic fever Diagnosis, treatment, Prevention, and control, 2nd ed. Geneva: World Health Organization, 1997.
- [24] E. Chungue, J.P. Boutin, and J. Roux, "Antibody capture ELISA for IgM antibody titration in sera for dengue serodiagnosis and survellance," *Research in Virology*, vol. 140, pp. 229-240, 1989.
- [25] F. Ibrahim, N.A. Ismail, M.N. Taib and W.A.B. Wan Abas, "Modeling of hemoglobin in dengue fever and dengue hemorrhagic fever using biolectrical impedance "*Physiol. Meas.*, vol. 25, pp. 607-615, 2004.
- [26] A.R. Herlina, I. Fatimah, and T. Mohd Nasir, "A non-invasive system for predicting hemoglobin (Hb) in dengue fever (DF) and dengue hemorrhagic fever (DHF) " in *Proc. Int. Conf. on Sensor and New Techniques in Pharmaceutical and Biomedical Research (ASIASENSE)*, Kuala Lumpur, 2005.
- [27] H. Abdul Rahim, F. Ibrahim, and M.N. Taib, "Modelling of hemoglobin in dengue infection application," *Journal of Electrical Engineering (ELEKTRIKA)*, vol. 8, pp. 64-67, 2006.
- [28] L. Albert, "Impedance ratio in bioelectrical impedance measurements for body fluid shift determinitation," in *Proc. Proc. of the IEEE 24th Annual Northeast Bioengineering*, 1998, pp. 24-25.

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