Malaria Parasite Classification based on Severity level:

A Comparative Evaluation of Sigmoid and Radial Basis Function

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Abstract

Malaria, one of the commonest life-threatening diseases in Africa, is caused by a single-celled parasite from the genus plasmodium. Once an individual gets infected by this parasite, the liver is first infected then the red blood cells. Malaria parasite if not properly diagnosed and treated in early stages might lead to severe conditions and even death. Detecting the levels of the malaria parasite from a thin blood smear becomes challenging when a lot of symptoms are present, and the inadequate approach is used. Hence there is a need for efficient classification of different levels of the malaria parasite in the human body in order to aid early treatment. This paper presents two classification model, a multi-layer perceptron neural network with sigmoid activation function and Radial basis function for classification of severity of Plasmodium Falciparumparasite into mild, moderate and severe levels using 17 features extracted of 500 observations from thin blood smear of patients. Dataset of malaria parasite patients is sourced from the Federal Medical Center, Ido-Ekiti, Nigeria. The work is implemented in MATLAB. The performance of the techniques is evaluated based on mean square error (MSE), confusion matrix and receiver-operating characteristic curve. A comparative evaluation of the multilayer perceptron model using sigmoid function and radial basis function model is carried out and results obtained shows RBF having an overall accuracy rate of 99.4% compare to MLP accuracy rate of 86.6%.

Index Terms —*Malaria parasite, Severity classification, MultiLayer Perceptron (MLP), Radial Basis function (RBF), Sigmoid function.*

1 INTRODUCTION

In Sub-Saharan Africa, one disease which has ravaged humanity and drained a fortune in its control and treatment is malaria. Malaria, yet a preventable disease at early stages, remains a recurring challenge. Malaria is caused by any of the four parasite species, namely Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, and Plasmodium ovale. Malaria like other diseases can be contacted in a number of ways. It can be transmitted by bite of an infective female Anopheles mosquito or through blood transfusion from infected persons and also through use of contaminated needles and syringes. However, there are cases of transmission through mother to child. Depending on the malaria parasite specie, there is usually a 7-30 day period within which the mosquito bite and appearance of early symptoms occur. Some common associated symptoms of malaria include fever, vomiting, headache, pain, chills, cough, sweating, myalgia, nausea and diarrhoea. Of the four causal species of malaria, Plasmodium falciparum is the most common, which if not detected and treated early can lead to prolonged state of unconsciousness, renal insufficiency and failure, or eventually death. Diagnostic test for malaria is through sample of blood smear (thin or thick) from a prospective patient. Early detection of malaria is important for its control. This aids the type of treatment administered and reduces chances of chronic state or death. Thus, classification of the severity of malaria parasite (Plasmodium falciparum) in patients is challenging and requires efficient approach. Classification of malaria parasite levels into mild, moderate and severe levels using neural network methodology forms the basis of this paper.

According to WHO World Health Malaria Report 2016, there are an estimated 212 million new cases of malaria and 429000 deaths in 2015 [1]. The WHO African Region bears the heaviest malaria burden with an estimate of 90% malaria cases and 92% related deaths in 2015. It is

reported that three quarters of these deaths are estimated to have occurred no fewer than 15 countries having Nigeria and Democratic republic of Congo accounting for more than a third. These alarming death statistics owing to malaria could be reduced by early detection of severity levels of the malaria parasite in patients. Classification of malaria parasite specie using thin and thick blood smear have attracted lots of attention in most literature. A combined algorithm consisting of morphological operations and colour-based pixel discrimination technique to identify malaria parasites from thick smear images of Plasmodium vivax is presented [2]. An important contribution of this paper is that the proposed approach requires no training set and assumes unsupervised methodology. The study in [3] shows that it is possible to achieve high quality standards in thick film malaria parasite counts by digital image analysis. The paper utilizes digital image processing and analysis systems in microscopic determination of malaria parasite load. One major constraint of digital image analysis as reported in the paper is the need to capture substantial numbers of digital images of the specimens, which is not difficult but is time-consuming. This paper [4] discusses the application of the multilayer perceptron (MLP) network to classify the malaria parasite into three species, namely Plasmodium falciparum, Plasmodium vivax and Plasmodium malariae. The MLP network compared back propagation algorithm with Levenberg Marquardt and Bayesian Rule algorithms. This work [5] presents an automatic device for both detection and classification of malaria parasite species on thick blood film. The proposed system is based on digital image analysis and featured with motorized stage units. In this paper [6], an automated classification system operating on digitized images of thick blood film has been developed to classify between Plasmodium falciparum and Plasmodium vivax malaria parasite species using support vector machine (SVM).

This paper proposes classification of malaria parasite (Plasmodium Falciparum) in thin blood smear based on severity level using multilayer perceptron based neural network. This paper further investigates classification performance of sigmoid activation function and radial basis function (RBF). The dataset used in this study contains 17 features of 500 patient observations. The target classification is in three classes, mild, moderate and severe. The performance evaluation of the two activation functions used in the MLP is analyzed based on mean square error (MSE) and ROC curve metrics.

The rest of this paper is organized as follows: Section 2 presents detailed review on malaria parasite classification and techniques used in classification. Section 3 describes the design approach for classification of malaria parasite in thin blood smear using multilayer perceptron network. Section 4 reports the experimental results and performance evaluationof the two activation functions. Section 5 concludes the study and suggests future areas of research.

2 RELATED WORKS

Malaria parasite detection is done using the extracted features from the blood smear (either thin or thick). Plasmodium is a small single celled organism responsible for malaria. Plasmodium is spread through a vector. The vector for the organism is a species of mosquito called Anopheles. There are two tests to detect the malaria parasite; i.e. thick and thin blood smear. The thin blood smear is used to determine the species of malaria parasite while thick blood smear is used to find the density of malaria parasite per microliter of red blood cell. In this paper, features extracted from thin blood smear are used in classification of severity level of plasmodium falciparum into mild, moderate and severe. Some related works on techniques used in classification of malaria parasite are presented.

This paper [4] discusses the application of the multilayer perceptron (MLP) network to classify the malaria parasite into three species, namely Plasmodium falciparum, Plasmodium vivax and Plasmodium malariae. The study used six features from thin blood smear. They include size of RBC infected per size of normal RBC, shape of parasite, number of chromatin, number of parasite per RBC, texture of RBC and location chromatin of parasite. Three different training algorithms, back propagation, Levenberg-Marquardt and Bayesian Rule algorithms are investigated to train the MLP networks in order to determine the applicability of the MLP network. In this study [4], the MLP network trained using back propagation algorithm produced the best performance with 89.80% accuracy as compared to Levenberg-Marquardt and Bayesian Rule algorithms. This paper y demonstrates the applicability of the MLP network for classifying malaria parasite species. In [7], the study shows that the chosen malaria rapid diagnosis test (RDT) performed superiorly in discriminating symptomatic malariacases with low parasitaemia than field microscopy, although it did not discriminate mixed infections. An RDT for malaria diagnosis may find a promising use in the Brazilian Amazon integrating a rational diagnostic approach. Despite the low performance of the MalDANN test using solely epidemiological data, an approach based on neural

networks may be feasible in cases where simpler methods for discriminating individuals below and above threshold cytokine levels are available.

An alternative approach useful for medical practitioners to detect malaria and accurately identify the level of severity is presented [8]. In this paper, the methodology is developed based on the Jordan–Elman neural networks. Its performance is evaluated using a receiver-operating characteristic curve, sensitivity, specificity, positive predictive value, negative predictive value, confusion matrix, mean square error, determinant coefficient, and reliability. The effectiveness of the classifier is compared to a support vector machine and multiple regression models. The performance evaluation between the proposed method, support vector machine and multiple regression models showed that better performance for the proposed Jordan–Elman neural network model.

An image processing algorithm to automate the diagnosis of malaria in blood images is developed [9]. The image classification system is designed to positively identify malaria parasites present in thin blood smears, and differentiate the species of malaria. Image features based on colour, texture and the geometry of the cells and parasites are generated, as well as features that make use of a priori knowledge of the classification problem and mimic features used by human technicians. The first order features provides the basic mathematical ranges for different types of parasites. A two-stage tree classifier distinguishes between true and false positives, and then diagnoses the parasite species of the infection.

In this paper [10], the authors propose a comprehensive image classification framework for malaria-infected stage detection using microscopic images of thin blood smears. The methodology consists of microscopic imaging of Leishman stained blood slides, noise reduction and illumination correction, erythrocyte segmentation, feature selection followed by machine classification. Amongst three-image segmentation algorithms (namely, rule-based, Chan–Vese-based and marker-controlled watershed methods), marker-controlled watershed technique provides better boundary detection of erythrocytes specially in overlapping situations. Microscopic features at intensity, texture and morphology levels are extracted to discriminate infected and non-infected erythrocytes. The work uses feature selection techniques, namely, *F*-statistic and information gain criteria for ranking. Five different classifiers, namely, Naive Bayes, multilayer perceptron neural network, logistic regression, classification and regression tree (CART), RBF neural network are trained and tested by 888 erythrocytes (infected and non-infected) for each features' subset. Performance evaluation of the proposed methodology shows that multilayer perceptron network provides higher accuracy for malaria-infected erythrocytes recognition and infected stage classification. Results show that top 90 features ranked by *F*-statistic (specificity: 98.64%, sensitivity: 100%, PPV: 99.73% and overall accuracy: 96.84%) and top 60 features ranked by information gain provides better results (specificity: 97.29%, sensitivity: 100%, PPV: 99.46% and overall accuracy: 96.73%) for malaria-infected stage classification [10].Proteomic analysis of Plasmodium falciparum parasites from patients with cerebral and uncomplicated malaria is presented [11]. To identify new CM-specific parasite membrane proteins, a mass spectrometry-based proteomic study is conducted and the protein expression profiles between 9 CM and 10 uncomplicated malaria (UM) samples are compared.

Artificial Neural Network methodology (ANN) is used for the diagnosis of the disease in the red blood cell [12].Features are computed from the data obtained by the digital holographic images of the blood cells and serve as input to the network, which classifies the cell as the infected one or otherwise. The paper determined various parameters by processing the holographic images of healthy as well as infected RBCs. The proposed method using ANN gives results almost from 90-100%. These results can be refined more by increasing the number of parameters and also the sample size of the data provided.

Multilayer perceptron model is described as a good non linear approximator with a power ability to lean well non linear system, and most of research was limited to a 3 layers MLP, by describing that 3 layers are sufficient to have good approximation [13]. In this paper model construction for solving supervised classification tasks in data mining was of interest. This paper present two model approach in classification of malaria parasite, Multilayer Perceptron (MLP) and Radial Basis Function (RBF) model approach. Construction is based on two phases: a preparation phase and an optimization phase. The first one describes a process of data cleaning, discretization, normalization, expansion, reduction and features selection. The second phase aims to optimize the set of weights based on their activation functions. An empirical illustration is carried out in order to validate the models and comparison between the two model classifiers was done.

3 METHODOLOGY

Multilayer perceptron network and Radial basis function network are both supervised training network. In this paper, RBF network with one hidden layer uses neurons

with RBF activation functions. Then one output node is used to combine linearly the outputs of the hidden neurons. The MLP network presented here has two hidden layers and the neurons (processing units) in different layers uses the same activation function. Activation function of each hidden neuron in a RBF network computes the Euclidean distance between input vector and the center of that unit. Activation function of each hidden neuron in a MLP computes the inner product of input vector and the weight vector of the connecting neuron.

3.1 Dataset Description and Pre-processing

The data is sourced from Federal Medical Center, Ido-Ekiti, Nigeria. It contains 18 features extracted from thin blood smear from 500 patient observations. The raw features in the collected data include sex, age, height, weight, blood pressure, body Temperature, total number of RBC per field, number of RBC infected field, number of normal RBC per field, number of ring form (early trophozite) per field, number of gametophytes per field, number of malaria parasite per RBC per field, number of chromatin dot per field, number of chromatin dot on cytoplasm of RBC per field, number of chromatin dot on membrane of RBC per field, number of chromatin dot on cytoplasm of malaria parasite, number of deformed infected RBC per field and Number of Malaria Parasite per RBC Field. The sex feature is removed from the study because it has little or no effect on classification performance. The features are detailed in Table 1.

Table 1 - Dataset Features Description

S/N	Feature Symbol	Feature Description
1	X_1	Age
2	X_2	Height
3	X_3	Weight
4	X_4	Blood Pressure
5	X_5	Body Temperature
6	X_6	Total Number of RBC Per Field
7	X_7	Number of RBC Infected Per Field
8	X_8	Number of Normal RBC Per Field
9	X_9	Number of Ring Form (Early Trophozites)
10	X_{10}	Number of Late Trophozites Per Field
11	X_{11}	Number of Gametocytes Per Field
12	X_{12}	Number of Chromatin Dot Per Field
13	X_{13}	Number of Chromatin Dot on Cytoplasm of RBC Per Field
14	X_{14}	Number of Chromatin Dot on Membrane of RBC
15	X_{15}	Number of Chromatin Dot on Cytoplasm of Malaria Parasite
16	X_{16}	Number of Deformed Infected RBC Per Field
17	X_{17}	Number of Malaria Parasite per RBC Field

In the pre-processing stage, the features are defined into ranges to aid proper input-output mapping with the activation functions in the neural network. The ranges include very low, low, average, high and very high respectively.

Table 2 - Features Pre-Processing

Feature Symbol	Very Low	Low	Average	High	Very High
X_1	-	15 - 30	30 - 45	45 - 60	60 - 75
X_2	-	0 – 1	1 – 2	2 – 3	-
X_3	10 – 30	30 – 50	50 – 70	70 – 90	90 – 110
X_4	-	70/40 – 90/60	100/70 – 139/80	140/90 – 190/100	-
X_5	-	36 – 37	37 – 38	38 – 39	-
X_6	128 – 228	228 – 328	328 – 428	428 – 528	528 – 628
X_7	12 – 24	24 – 36	36 – 48	48 – 60	-
X_8	80 – 178	178 – 276	276 – 374	374 – 472	472 – 570
X_9	4 – 19	19 – 34	34 – 49	49 – 64	64 – 79
X_{10}	0 – 6	6 – 12	12 – 18	18 – 24	24 – 30
X_{11}	0 – 1	1 – 2	2 – 3	3 – 4	4 – 5
X_{12}	18 – 33	33 – 48	48 – 63	63 – 78	-
X_{13}	12 – 22	22 – 32	32 – 42	42 – 52	-
X_{14}	0 – 2	2 – 4	4 – 6	6 – 8	8 – 10

X_{15}	0 – 4	4 – 8	8 – 12	12 – 16	16 – 20
X_{16}	0 – 4	4 – 8	8 – 12	12 – 16	16 – 20
X_{17}		0 – 1	1 – 2	2 - 3	

3.2 Multilayer Perceptron Model

Multilayer perceptron is the most prevailing neural network structure being use. MLP is a feed-forward network where synapses (connections) are made from an input layer, one or more hidden layers and an output layer [14]. In this paper, the network comprises of input layer x with 17 neurons (x_1, x_2, x_3. . . x_{17}), two hidden layer with 8 neurons each and an output layer with 3 neurons. Figure 1, shows the MLP network. At each hidden layer neurons, two functions are performed [15]. The combination function (weighted sum of the input values) is multiplied by the weights of the respective connections and a bias [16]. The activation function (determines the relationship between the input and output neurons).

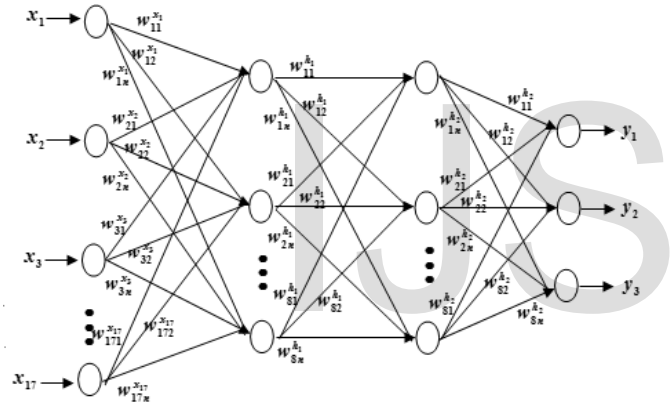

Fig 1: Multilayer Perceptron Network

The function for each first hidden neuron is defined by:

$$P_j^{h_1} = \sum_{i=1}^{n} x_i w_{ji}^{x_i} + b_j \qquad 1$$

$w_{ji}^{x_i} = (w_{j1}^{x_1}, w_{j2}^{x_2}, ..., w_{j17}^{x_{17}})$ is the weight connecting the input neuron j to the hidden neurons. The output is produced by applying activation function to $P_j^{h_1}$

$$y_j^{'} = F(P_j^{h_1}) = F\left(\sum_{i=1}^{n} x_i w_{ji}^{x_i} + b_j \right) \qquad 2$$

Second hidden layer neurons is defined by:

$$P_j^{h_2} = \sum_{i=1}^{n} y_j^{'} w_{ji}^{h_1} + b_j \qquad 3$$

$w_{ji}^{h_2} = (w_{j1}^{h_2}, w_{j2}^{h_2}, ..., w_{j8}^{h_2})$ is the weight connecting the previous hidden layer neuron j to the second hidden neurons.

Applying activation function to $P_j^{h_2}$, produced the output:

$$y_j^{''} = F(P_j^{h_2}) = F\left(\sum_{i=1}^{n} y_j^{'} w_{ji}^{h_1} + b_j \right) \qquad 4$$

Output of the Output layer neurons with applied activation function is defined by:

$$o_k = F\left(\sum_{i=1}^{n} y_j^{''} w_{ji}^{h_2} + b_j \right) \qquad 5$$

First, hidden layer neurons passes through the activation function (sigmoid function). The second hidden layer receives inputs from the preceding layer of neurons and passes the output on to the output layer.

Sigmoid function used at each hidden layers is given by:

$$f(P) = \frac{1}{1+e^{-P}} \qquad 6$$

Using the mean-squared error and with gradient descent method, weighting coefficient can be updated by.

$$\Delta w_{kj} = \eta (d_k - o_k) f_k'(P_k) o_j \qquad 7$$

Δw_{kj} is the weight update between the output neurons and the second hidden layer neurons.

$$\Delta w_{ji} = \eta \left[\sum_{k=1}^{n} (d_k - o_k) w_{kj} f_k'(P_k) \right] f_j'(P_j) o_j \qquad 8$$

Δw_{ji} is the weight update connecting the second hidden layer neurons and the first hidden layer neurons.

$$\Delta w_{hj} = \eta \left[\sum_{j=1}^{n} (d_k - o_k) w_{ji} f_k'(P_k) \right] f_j'(P_j) o_j \qquad 9$$

Where Δw_{hi} is the weight connecting the first hidden layer neurons to the input layer neurons and η is the learning rate.

3.3 Radial Basis Function

Radial basis function is a neural network that uses radial basis functions as activation functions [17]. RBF have one input layer, one hidden layer and one output layer. The hidden layer calculates the norm of the input from the

neuron. It passes the norm through a non-linear activation function [18]. In this research, RBF network has same number of neurons at the input layer, one hidden layer with 100 neurons (this is so has RBF continuous to increase the neurons at the hidden layer until error goal is reached), and 3 neurons at the output layer corresponding to three classes of malaria parasite. It's should be noted that when mean squared error goal is not set, RBF neural networks is stopped when the number of hidden layer neurons reached the maximum default value, which is the number of instances in the training data set [19]. The RBF network is shown in Figure 2

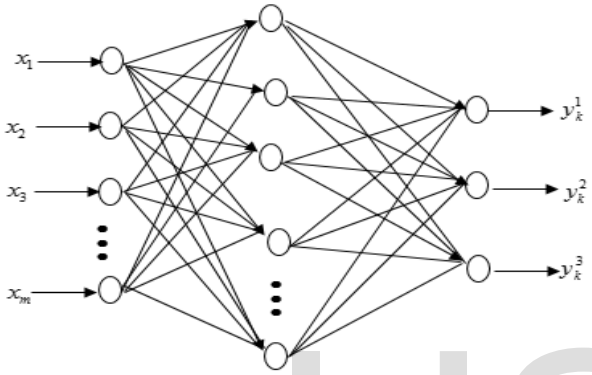

Fig. 2: Radial Basis Function Network

3.3.1 Learning Algorithm

RBF supervised learning algorithm for training are characterized by their mean vectors (centers), shapes(spreads) and weights [17].Here the network input to the radial basis activation function is the vector distance between its weight vector (center) and the input vector. The Gaussian equation used at the activation function is defined by:

$$f(x) = \frac{1}{\sigma_i \sqrt{2\pi}} e - \frac{(x-\mu_i)^2}{2\sigma_i^2} \quad 10$$

Where x is the input vector, σ_i , μ_i are the spread and center respectively. The spread is expressed:

$$\sigma_i = \frac{Maximus\ \ distant\ between\ any\ two\ centers}{\sqrt{number\ of\ center}} \quad 11$$

The connections between the hidden neurons and the output neurons are weighted sums. The output value $y_k(x)$ of the k[th] neuron is given by [20],

$$y_k(x) = \sum_{j=1}^{m} W_{kj} f(x) \quad 12$$

Where W_{kj} is the weight between neuron in hidden layer to k[th] neuron in output layer and $y_k(x)$ is the output of k[th] output layer neuron.

4 Performance Evaluation and Results

The evaluation metrics used in this study is Mean Square Error (MSE) for performance and a confusion matrix for classifier quality. Implementation is done using Matlab R2015a tool.

4.1 Performance Evaluation

The performance for the MLP and RBF is shown in table 3.

Table 3 - Performance

	Performance (MSE)	
	MLP	*RBF*
Training	0.0800	0.0034
Test	0.1151	0.0000306

Confusion table presented in Table 4 and Table 6 shows the number of correct and incorrect predictions made by the classification model for both MLP and RBF respectively, compared to the actual class in the data. With 20% (100 instances) test data, table 4 shows that 7 instances were correctly classified as mild, 5 instances of moderate were incorrectly classified as mild, 67 of moderate correctly classified as moderate, 6 instances of mild were incorrectly classified as moderate and 6 instances of severe were incorrectly classified as moderate. Also 3 of severe were correctly classified as severe while only 6 instances of moderate were incorrectly classified as severe. Moderate class has the highest classification rate (True Positive) as shown in table 5.

Table 4 - MLP Confusion Table for Test Data

		Actual			
Output Model	*Classes*	*Mild*	*Moderate*	*Severe*	*Total*
	Mild	7	5	0	12
	Moderate	6	67	6	79
	Severe	0	6	3	9
	Total	13	78	9	100

TP is the correctly classified outcome of the model to be true, when the actual class is true.

FN is the incorrectly classified outcome of the model to be false, when the actual class is true.

TP Rate = TP/ (TP + FN) 13

Accuracy = (TP_{Mild} + $TP_{Moderate}$ + TP_{severe}) / Total class number

MLP test Accuracy = (7+67+3)/100 = 77/100 =77

RBF Test Accuracy = (13 + 78 + 9)/100 = 100/100 = 100

Table 5 - MLP Class True Positive Rate

Class	TP Rate (%)
Mild	58.3
Moderate	84.8
Severe	33.3

Table 6 - RBF Confusion Table for Test Data

		Actual			
	Classes	*Mild*	*Moderate*	*Severe*	*Total*
Output	*Mild*	13	0	0	13
	Moderate	0	78	0	78
	Severe	0	0	9	9
	Total	13	78	9	100

With the same data instance used, RBF show better performance as compare to MLP. 13 of 13 were correctly classified as mild, 78 of 78 for moderate and 9 of 9 for severe. The true positive rate is shown in table 7.

Table 7 - RBF Class True Positive Rate

Class	TP Rate (%)
Mild	100
Moderate	100
Severe	100

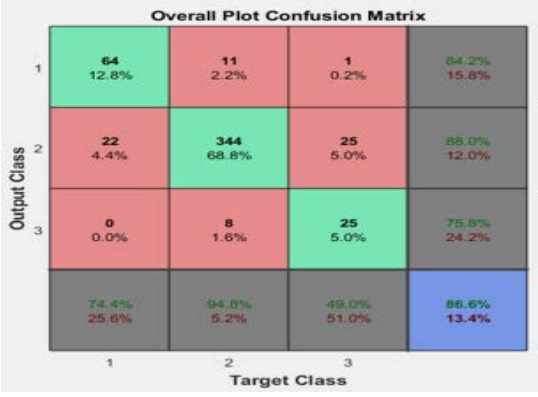

Fig 3: Overall Confusion Matrix for MLP

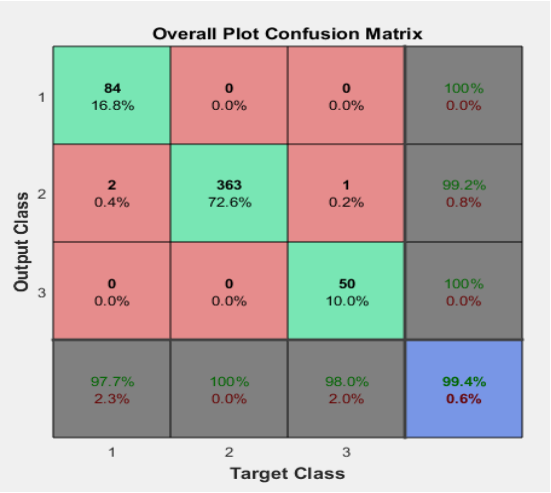

Fig 4: Overall Confusion matrix for RBF

Fig.3 and Fig.4, shows a 3 x 3 overall performance confusion matrix of the three target classes, the mild, moderate and severe, presented as 1, 2 and 3 respectively. The diagonal cells show the number of instances that were correctly classified, and the off-diagonal cells show the misclassified instances. The blue cell in the bottom right shows the total percent of correctly classified instances (in green) and the total percent of misclassified cases (in red) [21].

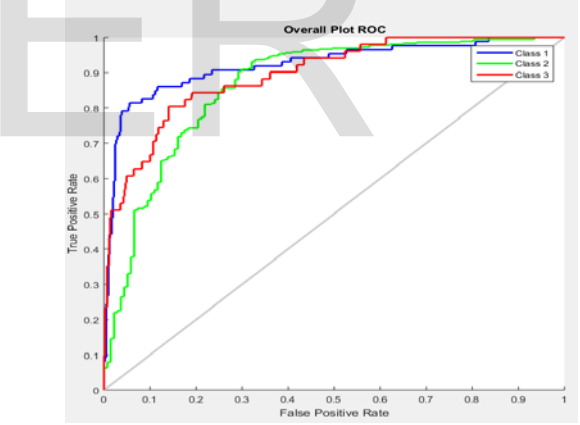

Fig 5: Overall ROC curve for MLP

The receiver operating characteristic curve (ROC) is a plot of the true positive rate versus the false positive rate as the threshold is varied [21]. Figure 5 shows MLP overall ROC curve for each classes are poorly classified as compare to RBF overall ROC curve, as each of the classes are almost perfectly touching the classification line as in shown in figure 6.

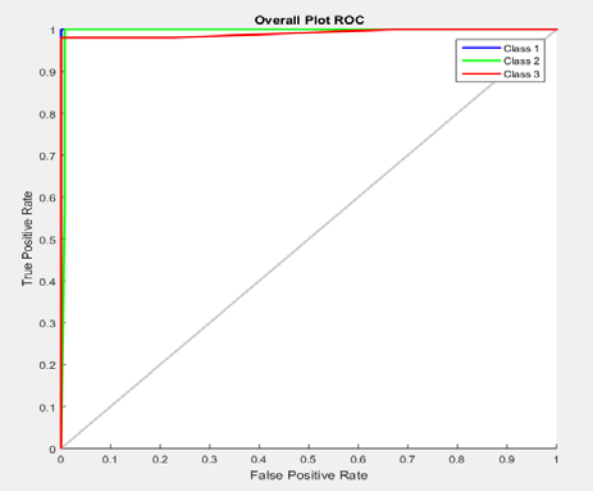

Fig 6: Overall ROC for RBF

Fig.7 and Fig.8 shows the test ROC curves for MLP and RBF respectively. RBF ROC curve for each classes completely touches the classification line, which means 100% accuracy.

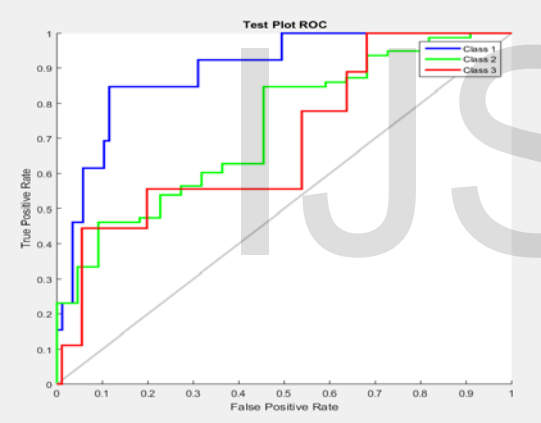

Fig 7: Test ROC for MLP

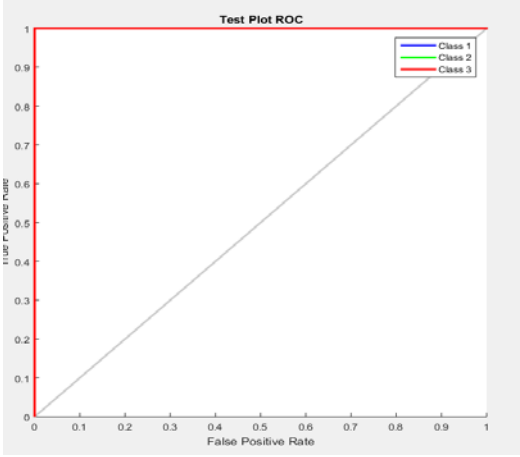

Fig 8: Test ROC for RBF

4.2 Discussion of Results

Radial basis activation function and Multilayer neural network uses different activation function at the hidden layer neurons. In this study, RBF has shown superior classification ability compared to MLP. Overall accuracy for RBF gives 99.4% compared to MLP with 86.6%. We tested the two models with 20% of the data acquired, and RBF accuracy gives 100% and MLP has 77% accuracy. This show that BRF activation function best hits the target compares to MLP sigmoid function. Best hit is shown with the RBF ROC curves in figure 7 and 8 as the point is at the left comer compare to MLP ROC curve in figures 4 and 5.

5 CONCLUSION

Multilayer neural network and Radial basis function are both, non-linear feed-forward networks, universal approximators and could be used in similar application areas. They both uses different activation function at their hidden layer. In this paper, we have been able to select an optima network architecture for both models, experiment with the acquired dataset with a reasonable instances. From the result obtained, RBF with basis activation function has better classification ability compare to multilayer perceptron sigmoid function. In this study, the choice of number of hidden layer(s) neurons for MLP was to avoid computational complexity as training iterations get increased with more neurons. RBF training iterations is limited to the number of input instance or upon specified set goals. Both optimised networks provide reasonably good results.

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