Application of Artificial Neural Network for Diagnosis of Cerebrospinal Meningitis

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Abstract

The non-systemization of meningitis diagnosis procedures introduces varying degrees of subjectivity at different stages in the process. This reduces final objectivity of accuracy and increases diagnosis time. To reduce the effects of these shortcomings, an Artificial Intelligence (AI) method for automatic diagnosis of meningitis from gram-stained sputum smear microscopy images, using image processing techniques and Artificial Neural Network (ANN) is presented in this research. An intelligent method of meningitis diagnosis through the application of ANN using image processing techniques was achieved through blood samples collected from the patient and placed in a special dish for microorganism growth observation particularly bacteria. Extraction of image data for cerebrospinal fluid (CSF) sample from the patients were also investigated for meningitis. Segmentation by cascade adaptive threshold-based approach was used to segment meningitis bacilli by pixel intensity value due to gram-staining. A multi-layer (ML) ANN with scaled conjugate gradient descent back propagation training algorithm was used to finally classify the presence or absence of TB bacilli in the pre-processed input image.
MATLAB image processing and Neural Network Toolboxes was used to simulate the procedure. Results of the ANN classifier gave a Mean Square Error (MSE) of 0.025 and accuracy of 94.7%. These results showed that image processing can help to detect the presence or absence of meningitis bacilli in gram-stained CSF smear samples.

Keywords: Multi-layer Artificial Neural Network, Artificial Intelligence, Meningitis

1.0 INTRODUCTION

Diagnosis is a process of identification of a condition, disease, disorder or problem by systematic analysis of a background or history, examination of signs or symptoms, evaluation of the research or test result and investigation of the assumed or probable causes (Suzuki 2011). It involves the analysis and interpretation of the obvious or procured data relevant to the condition with a view to arriving at a conclusion, so that effective remedy can be administered to achieve a healthy state. The bulk of word and practice in the field of medicine is built around it. Normally, diagnosis is carried out by expert Physicians, who in addition to consideration of patient's bio history and physical examinations also use laboratory results, X-rays and scans to determine the correct ailment. Issues may arise due to the manual interpretation of test or scan results making the procedure slow and subject to human errors. One possible alternative is to use artificial intelligence techniques to automate the diagnosis procedure. In particular, ANN can be used to automate the procedure partially or fully (Suzuki 2011).

With the growing concern about faster and efficient methods of diagnosis in biomedical Engineering, ANN with the help of image processing techniques can be deployed in medical diagnosis especially in diseases that are of medical emergencies and public concerns such as meningitis. ANNs are mathematical techniques which can be used for modeling human brain, also for data categorization and inference tasks in any empirical science. This means that they have a two-fold interest for the philosopher. Firstly, ANN theory could help to understand the nature of mental phenomena such as perceiving, thinking, remembering, inferring, knowing, wanting and acting. Secondly, because ANNs are such powerful instruments for data classification and inference, their use also leads into the problems of prediction, induction and deductions. It adds up simple functions in a way that gives it the ability and flexibility to universally approximate functions. The ANN can approximate any continuous mapping with arbitrary precision, these attributes have given it wide and successful applications in various fields and disciplines such as control, sciences, industry, economics, medicine and social sciences. In the field of medicine, it has found application in the different sections of health care administration especially in stages of diagnoses (www.data-machine.com), (Haykins 1999).

Meningitis is inflammation of the protective membranes covering the brain and spinal cord. The inflammation may be caused by infection with viruses, bacteria or other microorganisms, and less commonly by certain drugs. Meningitis can be life-threatening because of the inflammation's proximity to the brain and spinal cord; therefore the condition is classified as a medical emergency (Encyclopedia Britannica, 2012), (www.cdc.gov/), (www.news-medical.net/).

Organisms causing meningitis were identified in the late 19th century to include *Streptococcus pneumonia*, *Neisseria meningitidis*, *and Haemophilus influenza.* If a rash is present, it may indicate a particular cause of meningitis; for instance, meningitis caused by *Neisseria meningitides* may be accompanied by a characteristic rash consisting of petechiae on the trunk, lower extremities, mucous membranes, conjuctiva, and (occasionally) the palms of the hands or soles of the feet. Meningitis outbreak was first recorded in Geneva (Switzerland) in 1805. (www.cdc.gov/).

In Africa, the first outbreak was described in 1840 (www.news-medical.net/). African epidemics became much more common in the 20th century. The first major one was reported in Nigeria and Ghana in 1905–1908. In early reports large number of people died of the disease (www.cdc.gov/). Recently, the outbreak of Cerebrospinal Meningitis, (CSM), in Nigeria is repetition of series of outbreaks mostly affecting states in the upper parts of the country which fall within the African Meningitis Belt (www.voiceofmeningitis.org/). One of the worst occurred in 1996 when 109,580 cases and 11,717 deaths were recorded. In 2003, there were 4,130 cases and 401 deaths; 9,086 cases and 562 deaths were recorded in 2009. The historical records and past experiences influenced health authorities in Africa (especially countries within the African Meningitis Belt), the World Health Organization and Development Partners to roll out a strategic intervention for the effective prevention of such epidemics (www.who.int/mediacenter/). The affected states in Nigeria include Zamfara, Katsina, Sokoto, Kebbi, Niger, Nassarawa, Jigawa, FCT, Gombe, Taraba and Yobe. Others are Kano, Osun, Cross Rivers, Lagos and Plateau.

In biomedical applications, diagnosis is an essential part which can be used to know the status of the patient ailment. The result of this research tends to improve the accuracy of the diagnosis by the use of Artificial Neural Network and image processing techniques.

1.1 MEDICAL DIAGNOSIS

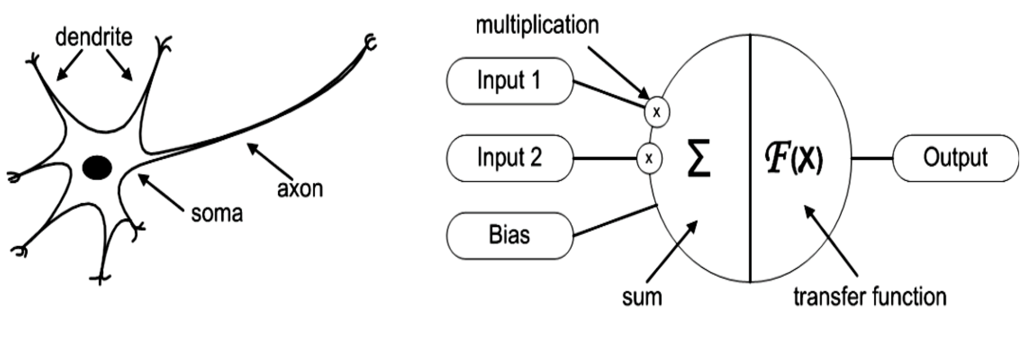
Medical diagnosis is the term used to describe the conclusion arrived by an expert Physician on the cause of a patient’s ailment. It is established on the analysis and interpretations of result from patient's history, examinations and tests samples taken from the patients. The procedure involves three major stages: patient history, physical examination and tests (Suzuki, 2011).

1.2 MEDICAL DIAGNOSTIC SAMPLES

Various principles, methods and tools are applied for the different diagnostic stages. For tests, samples and result are classified according to: Sample location and type; which, inform where the sample is taken from the patient's body such as blood, urine, stool, sliver and cerebrospinal fluid. For this work, the sample is cerebrospinal fluid taken from the spinal cord of the patient. Others include: methods/Microbiological culture used to process and obtains results such as physical examination, taking medical history, radiological tests (X-rays, Computer Tomography CT scans etc.) and utility i.e. the usefulness of the result. For this research, the test result is for the purpose of preliminary diagnosis. Result from the tests on patient samples is able to give or show necessary confirmatory or negating information to conclude on the type of ailment. The fact gleaned from patient history and physical examinations sometimes are vague with lots of gaps in the information gathered making correct diagnosis slow and difficult. This has put much focus on the research and development of the test's stages in the medical diagnosis procedure. (Suzuki, 2011).

1.3 ARTIFICIAL NEURAL NETWORK (ANNs)

An artificial neural network is an interconnection of artificial neurons in a parallel information-processing structure that attempts to emulate certain performance characteristics of the natural human biological neural system (Abdulsalam *et al,* 2016). The biological neuron has three components that are of interest in understanding the operation of its artificial counterpart. These are the dendrites, soma and axon. Figure 1 illustrates a generic biological neuron and Figure 2 is a model representation of neuron (Haykins, 1999), (Suzuki, 2011) (Bishop, 1995). A human neuron cell has a cell body which is called the soma, an axon and dendrites. The axon is a long cylindrical connection that carries impulses from the soma of the neuron to the dendrites. The axon ends in dendrites (output dendrites), the contact area between these dendrites and that of another neuron, the synaptic gap. The receiving neuron either generates an impulse to its axon, or produces no response. These signals may originate from a variable, such as chemical, electrical, temperature change, they have to cross the synaptic gap by chemical process.



(a) **(b)**

Figure 1: Simple representation of Biological Human Neuron (Suzuki, 2011)

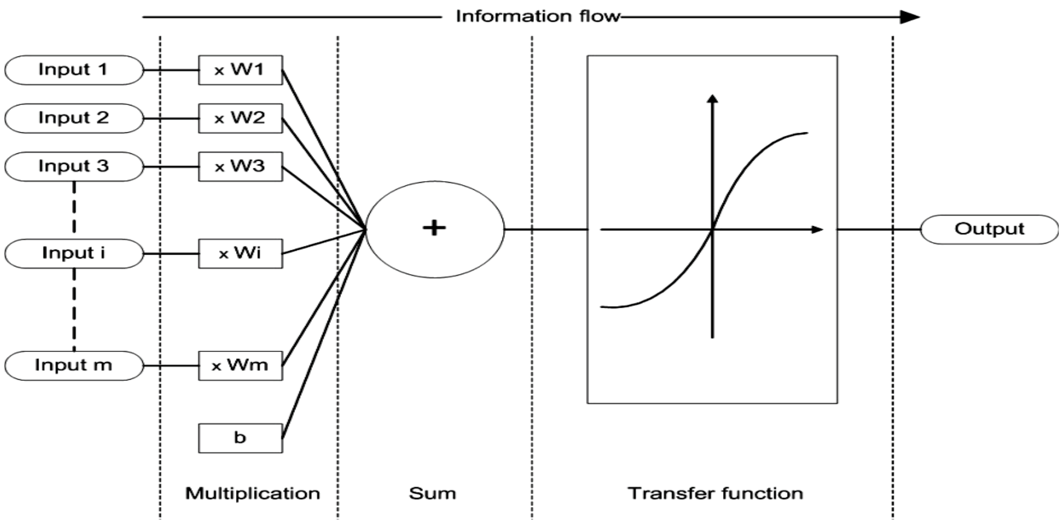


Figure 2: Representation of Artificial Neuron (Blahuta *et al.,* 2011)

2.0 RELATED WORKS

Mimicking the parallel data/information processing of natural biological neural network has given the ANN the ability to add simple functions such that it can approximate any continuous mapping with arbitrary precision (Paulo *et al,* 1999). This intrinsic property of the ANN has enabled it to achieve performance accuracy when compared with expert opinions or outcomes of conventional statistical method (Suzuki, 2011). This has made it applicable as a tool in a diversity of fields and disciplines. In the medical field, its application in the diagnosis of meningitis is receiving much attention with a view to improving sensitivity and speed of diagnosis. Several studies in researches and developments on the use of ANNs in the diagnosis of meningitis (or meningitis related ailments) have employed different methods and ANN structures.

In the work of (Ali *et al.,* 1999), active pulmonary Tuberculosis (TB) was diagnosed and predicted using ANN. Radiometric broth medium with auramine-rhodamine fluorescent stain were used to detect acid fast organisms on respiratory specimens. The ANN used was general regression neural network with multilayers. The result showed the ANN has a performance index with MSE of 0.009, sensitivity of 100%, specificity of 72% and 92.3% diagnosis accuracy.
(Orhan et al., 2010) developed ANNs to diagnose chest diseases among which was TB. They used multilayer neural network (MLNN), Probabilistic neural network, learning vector quantization (LVQ) neural network, Generalized regression (Bayesian) neural network, and Radial basis function neural network for diagnosis. The classification accuracy of chest disease for the different neural networks used ranges between 84% and 90% inclusive.

In (Blahuta *et al.,* 2017), brain-stem (which is also part of meningitis) was diagnosed with an ANN using image processing on finite set brainstem ultrasound images. They used the method of principal component Analysis (PCA) with C# programming language as a desktop application. Also, (Ibnu *et al.,* 2012) developed ANN for the identification of Tuberculosis. They used colour segmentation based on intensity values, de-correlation stretching, morphological shape, descriptors of eccentricity and compactness to isolate TB bacilli from images of Ziehl Nelson (ZN) prepared sputum smear samples. 929 TB bacilli shapes based on eccentricity and compactness were used to train the neural network. The performance index showed 88% accuracy.

Er *et al.* (2010) used a multilayer and generalized regression neural networks for TB diagnosis. They used the presence of 38 features to train the networks and reported about 93.3% accuracy for their generalized regression neural network, and 95% accuracy for the multilayer neural network with two hidden layers, and trained with Levenberg Marquard algorithm.

2.1 ANN TOPOLOGIES AND ARCHITECTURES

The connection of the artificial neurons in various ways based on principles and techniques give rise to ANNs having different topologies or architectures. Topologies are divided into two basic classes: Feed-Forward Neural Networks (FFN) and Recurrent Neural Networks (RNN). For easier handling and mathematical description, the individual neurons of an ANN are grouped in layers as also shown in Figure 3. The layers are classified as input, hidden and output layers (Blahuta *et al.,* 2011), (Howard and Mark, 2011). In some other design descriptions and groupings, the input is not considered as a layer, leaving only the hidden and output layers (Graupe, 2013)

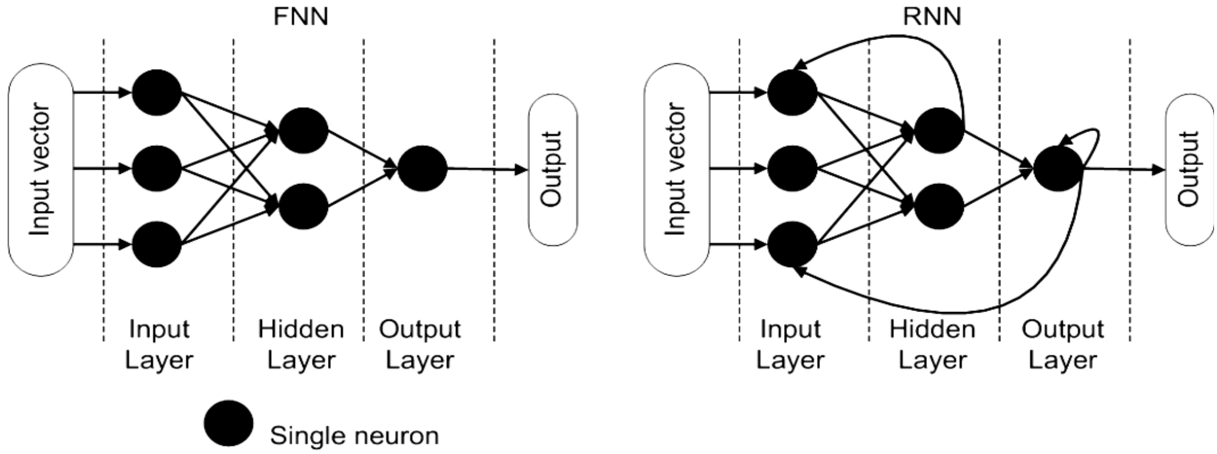


Figure 3: Feed-Forward (FNN) and Recurrent (RNN) Topologies of Artificial Neural Networks (Blahuta *et al.,* 2011)

The architectures can be further subdivided into two main classes based on the number of layers of processing nodes used in the model. In a single-layered network there is a layer of input nodes and a layer of output nodes, which are the only processing nodes in the model. In multi-layered network there are one or more hidden layers (Blahuta *et al.,* 2011). The choice of a particular topology is based on the problem. The ability of neural network to handle non-linear and complex problems lies in its hidden layers and the number of neurons in them. The more complex the problem to be solved, the more the need for more hidden layers to handle the complexity, although for most practical purposes, problems that require more than two hidden layers are rarely met (Suzuki, 2011), (Blahuta *et al.*, 2011), (Wilamowski, 2003). Table 1 summarizes the relationship between complex degree of problem and the number of hidden layers.

Table 1: Summary of relationship between problems and the number of hidden layers

Complexity of problem	No. of Hidden Layers in ANN Design
Linear problems	-
Practical (Real life) complex problems	1
Hypothetical-theoretical complex problems	2 and above

The number of neurons necessary in the input and output layers is determined by the number of vectors of features necessary to completely capture the problem to be solved (Baum and Haussler, 1989), (Suzuki, 2011), (Heaton, 2011). The number of neurons in the output layer is determined by the nature of the system. The number of neurons required in the hidden layer in order to accomplish a given task is a very critical issue in the ability of the network to solve the problem it is designed for. Having too few neurons in the hidden layer can result in under fitting by the network and too many neurons on the other hand can result in over fitting by the network (Wilamowski, 2003). Bias nodes having a constant output (usually of value =1) are often added to the input and hidden layers to give biasing to the network summation function.

3.0 METHODOLOGY

In this section, the algorithm developed and used for the implementation of the proposed method of diagnosis of meningitis of the brain infected by bacterial, fungal and or viral meningitis is elaborated on. The methodology consists of the following major stages: Data acquisition, pre-processing of data, training, validation and testing of adopted ANN. Each of these five stages is explained in detail in the subsequent sub-sections. The main procedure for meningitis diagnosis using ANN in this study is shown in Figure 4.

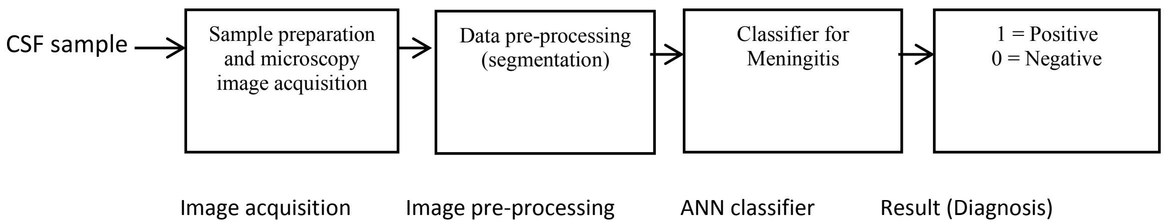


Figure 4: The Block Diagram of ANN algorithm development used for meningitis diagnosis.

3.1 SAMPLE PREPARATION AND MICROSCOPY IMAGE ACQUISITION

The raw data for the study were cerebrospinal fluid (CSF) samples being investigated for meningitis infection of the brain. The stained samples were obtained from the Department of Microbiology, Aminu Kano Teaching Hospital (AKTH) Kano. The camera capture of the microscopies of stained sample slides was carried out at the Department of Pathology of the same hospital. Verified and confirmed/validated (both positive and negative) color image samples were selected. Each sample was selected and prepared as described in the following subsections. In the Aminu Kano Teaching Hospital Microbiology Department, CSF samples for meningitis bacilli detection were prepared based on the gram staining technique. It is a technique that is used to apply standard medical stains and counter color on CSF smears to enable the detection of meningitis bacilli if present when the sample is viewed with a light microscope. It involves 0.01ml of the CSF samples being smeared in an area of 200mm^2 on typical frosted ended slides and then being flooded with Gram carbon fuchsin reagent as a primary stain. After that it is heated to steam point, rinsed in clean running water, re-flooded with a decolonization solution and re-rinsed with clean running water. It is then flooded with a counter-stain of methyl blue, rinsed, drained, and finally allowed to air dry (Pennwalt, 2007).

The air-dried sample slides were examined using a Zeiss Axiophoto photomicroscope with a high sensitive digital camera attached. Each sample was carefully examined manually and based on chosen number of fields before being captured by the mounted attached camera (specifications: Olympus U-TVO 63XG 7E/1089, Japan). This gave image of size 1536 x 2048 pixels which could be viewed on screen as well as being stored in a computer. Figure 5 shows a section of the color images of samples obtained.

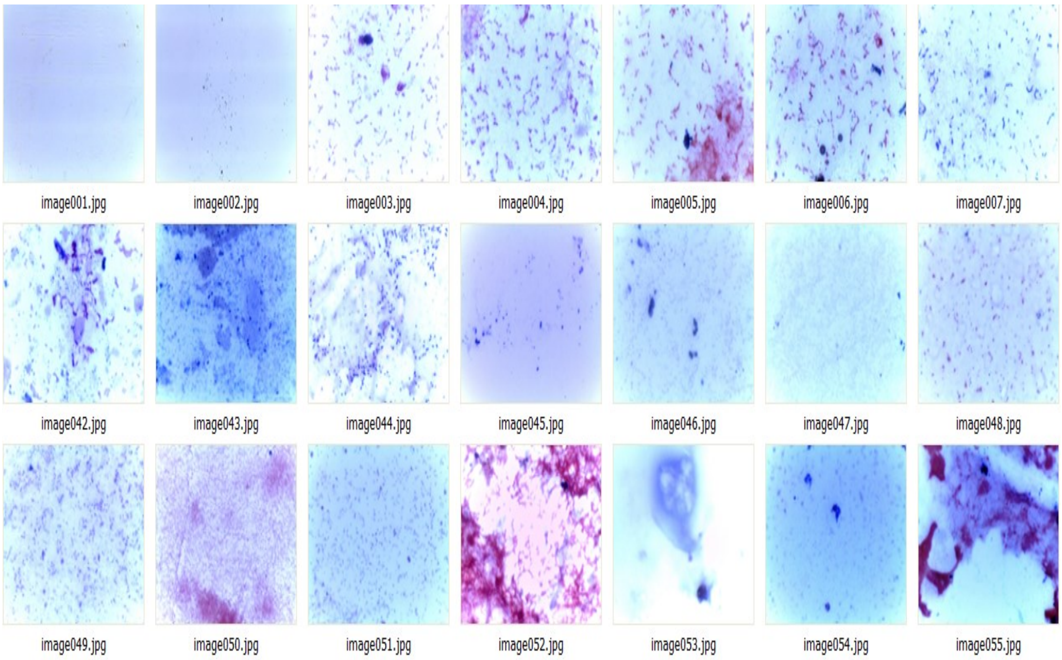


Figure 5: Gram stained color images of CSF Samples investigated for Neisseria Meningitis

3.3 MULTI-LAYER (ML) NEURAL NETWORK STRUCTURE

The ML neural network used has an input layer with hundred (100) inputs to handle hundred (100) input features. It has one single hidden layer with 30 neurons having tansigmoid activation function. Tansigmoid activation was used for its ability to accommodate inputs from minus infinity to plus infinity and output continuous value bounded between 1 and -1. In the adopted ANN the tansigmoid activation function was used in order to accommodate the range of inputs from feature extraction without the network experiencing output saturation (Gonzalez and Woods, 2002). The choice of the number of input vectors was determined by the available data for the problem, the number of output neurons was defined by the nature of the system while the number of hidden layers, the number of neurons in the hidden layer was determined by constructive direct method. The ML neural network is shown in Figure 6.

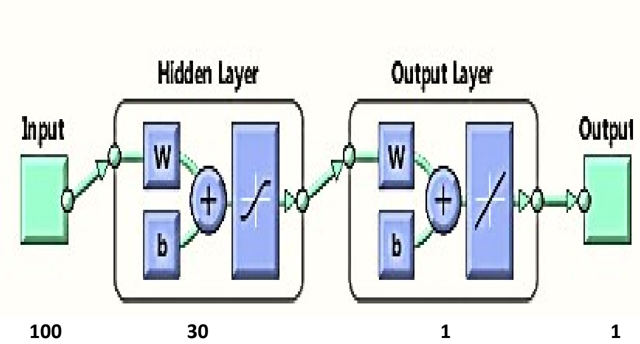


Figure 6: Architecture of one-layer ML Neural Network

3.4 DATA PARTITIONING

The sample input data and targets have to be divided into a training set, validation set and test set. For this study to achieve an optimal value of network performance after training a partitioning of 70% for training, 15% for validation and 15% for testing was used on the whole data set. This was to have the network exposed to more training samples, as larger training samples tend to enable the network generalize better on test data. The set of input data samples used to make the network learn by the computation of performance gradients and updates of weights and bias while validation was used to check for the best weights and bias when the validation set error is minimum in order to stop training based on the error profile. Finally, test set consists of samples which are used to measure the network's performance. The data partitioning window from the MATLAB Neural Network toolbox is shown in Figure 7.

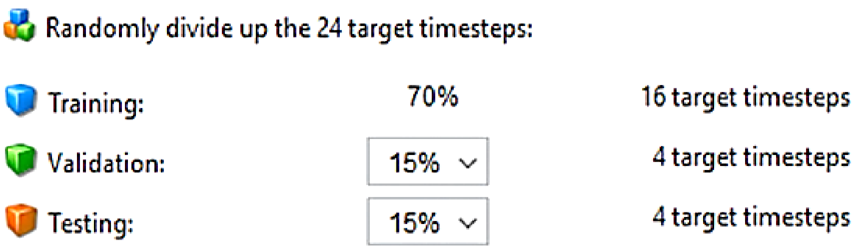


Figure 7: Data Partitioning Window of MATLAB Neural Network Toolbox

4.0 FEATURE EXTRACTION

The results from feature extraction stage showed the blob analysis used was successful as numerical values of feature variables considered bacilli objects were obtained in a 38 x 100 feature matrix that was used to train the ANN to classify with an acceptable degree of accuracy. A section of the extracted feature variables is shown in Table 2.

Table 2: A Sectional of Extracted Feature Variables of sample images

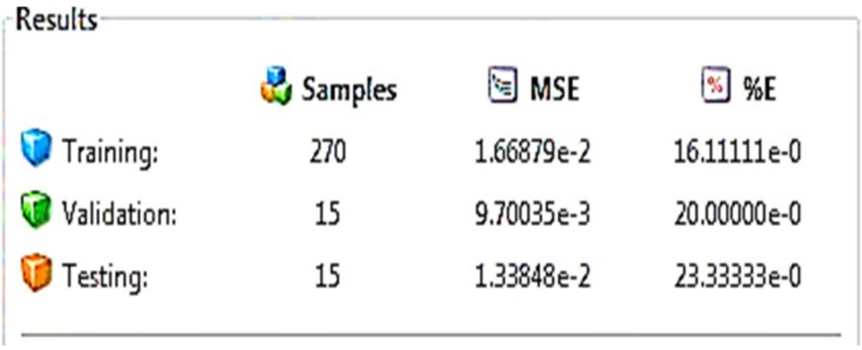
Sample Image	X1	X2	X3	X4	X5	…	…	…	…	X96	X97	X98	X99	X100
001	72	580	67	0	0	.	.	.	.	0	0	0	0	0
002	316	215	147	0	0	.	.	.	.	0	0	0	0	0
053	279	0	0	0	0	.	.	.	.	0	0	0	0	0
058	101	421	54	1234	108	.	.	.	.	94	32	28	123	66
049	91	857	281	260	51	.	.	.	.	53	38	25	26	0
007	0	0	0	0	0	.	.	.	.	0	0	0	0	0
046	174	224	1913	471	197	.	.	.	.	30	42	47	239	343
047	0	0	0	0	0	.	.	.	.	0	0	0	0	0
051	1397	188	246	59	104	.	.	.	.	388	100	46	58	39
049	95	67	0	0	0	.	.	.	.	0	0	0	0	0

4.1 RESULTS FROM ADOPTED ANN

The pre-processed input gave a matrix of size 38 x 100 for 38 sample images based on the data partition used - 28 for training, 4 samples for validation and 6 samples for testing. Results obtained are presented in the following subsections.

4.1.1 MEAN SQUARE AND PERCENTAGE ERRORS

Mean Square Error (MSE) value is among the parameters used in evaluating the final performance of an ANN. It measures the average squared differences between the output and targets. An ideal situation is to have zero differences. However, in practice a very small amount of error is tolerated. The percentage error on training set was 16.11% while the MSE of the performance was 0.0167. The percentage error on validation data was 20%, the MSE was 0.0970, also the percentage error on test data was 23.3% and MSE of 0.0134 was obtained. Figure 8 shows the results.


Results

	Samples	MSE	%E
Training:	270	1.66879e-2	16.11111e-0
Validation:	15	9.70035e-3	20.00000e-0
Testing:	15	1.33848e-2	23.33333e-0

Figure 8: MATLAB window showing ANN Training Results of MSE and Percentage Error

4.1.2 VALIDATION PERFORMANCE PLOT

This plot measures the performance of the ANN during validation in terms of MSE on a log scale. It shows how the performance is improving during training. It rapidly decreases as the ANN is being trained showing that the ANN is learning. The plot is shown for all the data set used for the training (training, validation and testing). The best validation performance MSE was 0.0026 at epoch 14 of ANN training. The performance plot is shown in Figure 9.

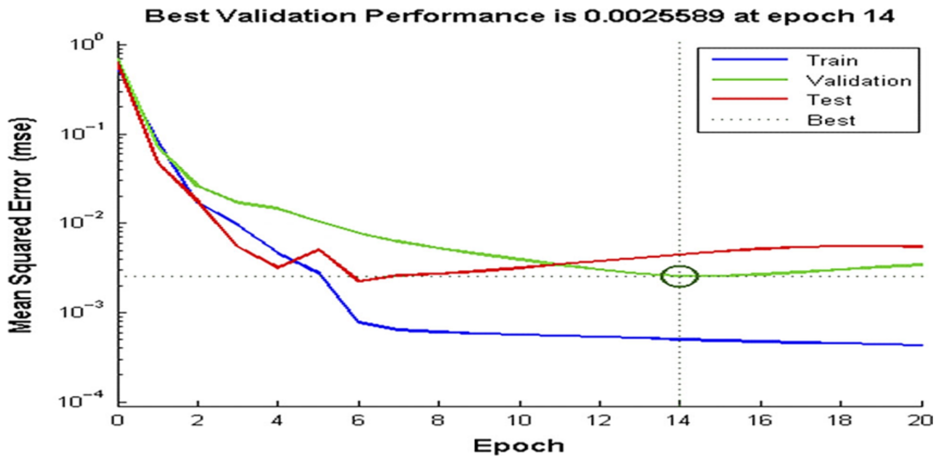


Figure 9: Best Performance Plot

4.1.3 GRADIENT AND VALIDATION PLOTS

Gradient and validation plots are used to assess the performance of ANNs during training. They show the profile of the networks in relation to the error gradient and at what epoch, also the best validation error and at what epoch during validation checks. On training the ANN for this study, the gradient was 0.0112 and validation was 6 both at the 21^{st} epoch. These are shown in Figure 10.

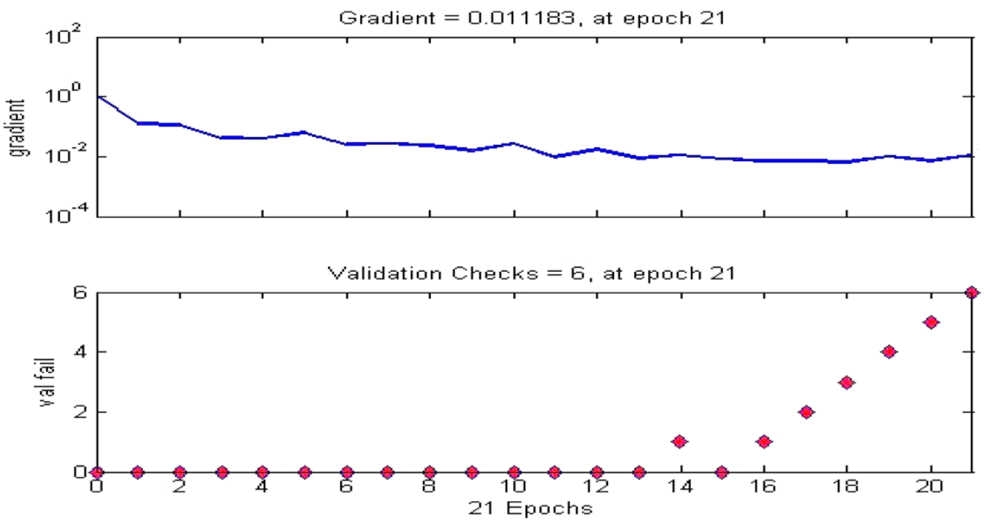


Figure 10: Gradient and Validation Plots of Training

A measure of how well the ANN classifies data was obtained through evaluation of its Receiver Operating Characteristics (ROC) plots. The plot is of true positive classifications (sensitivity) against false positive classifications (specificity) (Veropolous, 2001).
where

$$\text{Sensitivity}=\frac{Positives\ correctly\ classified}{Total\ Positives} \quad (1)$$

and

$$\text{Specificity}=\frac{Negatives\ correctly\ classified}{Total\ Negatives} \quad (2)$$

For a given output threshold, the area under the ROC curve is a powerful index for measuring true classification performance merit, its increase towards the top left corner gives a large area under the curve and a very small or zero error rate. This translates to sensitivity of almost 100% and specificity of approximate zero (Veropolous, 2001), (Gonzalez and Woods, 2002). Figure 11 shows ROC curves of training, validation and testing for the ANN classifier. The results demonstrate nearly zero area above the curves and large area under which means maximum classifier accuracy.

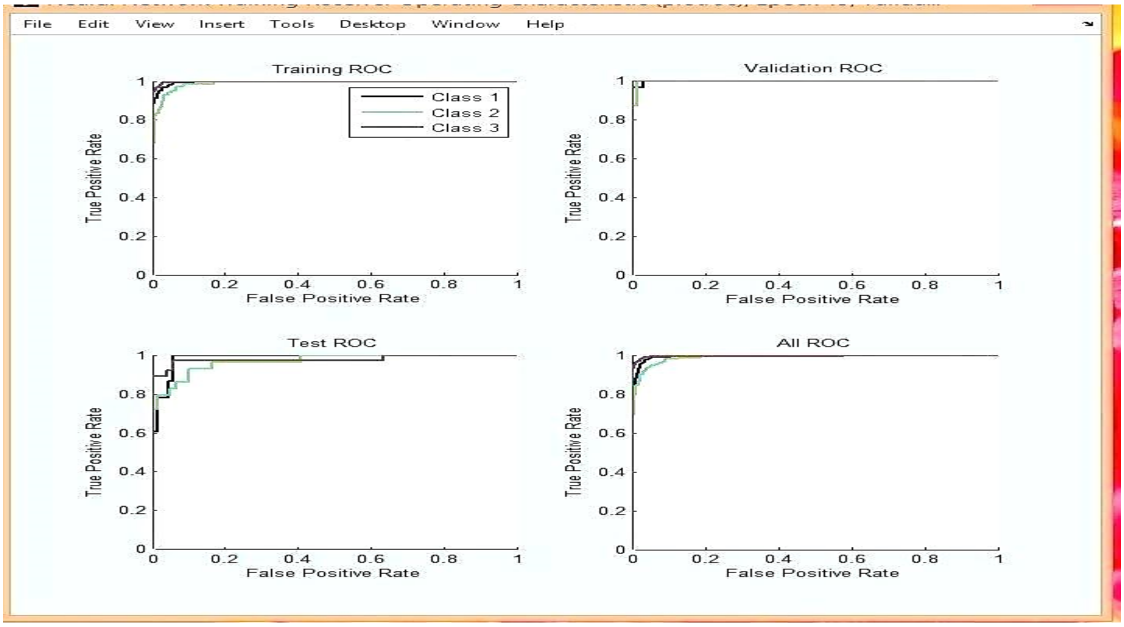


Figure 11: Result of Receiver Operating Characteristics plots

In addition, a confusion plot is also used to measure how well the ANN has classified the given data. It shows the percentage of correct and incorrect classifications with colored squares plotted across all the sample sets. Corrects classification percentage are given in green squares of the matrices diagonal. Incorrect classifications are given in red squares. The total or overall classification of correct and incorrect is given in the blue square. If the ANN has learned to classify properly the percentage in the red square will show very small values indicating few misclassifications. The confusion plot of the developed ANN gave an overall correct classification of 90% with 20% incorrect classifications as shown in Figure 12.

Figure 12: Results of Confusion plot

4.4 ANN TRAINING

The training applied to the developed neural network involved iterating epochs of the training set. An epoch by means of passing all input samples once was employed. Error adjustments were made using all inputs weights. At intervals, checks were made by passing a validation set, checking the error value, and finally passing the test set to see the generalization error measurement. The scaled conjugate gradient algorithm was automatically implemented by the neural network toolbox, training function, to achieve weights which will give minimal or zero error for optimal performance measure, MSE, for the input vectors of the given problem.

5.0 DISCUSSION OF RESULTS

The values of the different ANN performance evaluation parameters support and verify one another. The MSE value of 0.0250, the area above the ROC curves, and the confusion plots show acceptable accuracy values. This highlights the fact that given non-linear arbitrary inputs features which have been reduced to numerical form, the ANN can offer a good classification for meningitis diagnosis as shown by results obtained. In the manual procedure, the first thing the clinician does is identify the presence of meningitis bacilli in a sample based on color information. This fundamental function is implemented by segmentation based on color information used in the study method. After segmentation the images are black due to the absence of pixel values that fall within meningitis bacilli detecting pixel values used, while others will show white patches of mostly meningitis bacilli objects in a black background to indicate the presence of meningitis bacilli. The results obtained after implementing the segmentation procedure show that the method is rugged to absorb some of the problems that affect the quality of images from gram staining stages. A fixed threshold value cannot be adequately used to process the sample images, while the proposed cascade adaptive thresholding method applied produced stable, reproducible results across all samples. This stability plays fundamental stage in the diagnosis procedure.

5.1 CONCLUSIONS

The study is concerned with the diagnosis of Neisseria Meningitis through application of ANN using image processing techniques. The research result shows that with the incorporation of an image processing stage along with an ANN, more meningitis cases will be objectively confirmed positive or negative with high accuracy. In this case early medication can be administered to curb the infection. Results from segmentation showed that the techniques can be used to isolate Neisseria Meningitis from Cerebrospinal Fluid in the positive image of CSF samples after Gram staining. Based on the pre-processing of image of CSF sample which were used as inputs into the adopted ML neural network, the performance of the system gave an MSE value of 0.0250 and correct classification accuracy of 94.7% which can be interpreted that the ANN can classify i.e. diagnose positive or negative case of meningitis very quickly with a high degree of accuracy. Comparing the confirmed and verified image sample inputs (100%) with this measure of accuracy, gives the procedure an acceptable standard or validation. The proposed meningitis diagnosis structure is simple and can be adopted easily.

5.2 FUTURE WORK

From these research findings and the results obtained, ANN can classify Neisseria Meningitis based on training to recognize the bacilli features precisely. The crucial issue is how to also automate the procedure from obtaining CSF sample of patients being investigated for meningitis to preparation in order to achieve sameness of sample slide preparations. Achieving this step will be a major breakthrough for the fast and accurate diagnosis of meningitis. From the results obtained, the same segmentation technique can be used to isolate other disease-causing microbes (e.g. yeasts) in CSF samples after appropriate staining as a fundamental step in the bid to automate their diagnosis. Also the proposed techniques with some modification can be applied for forensic investigations.

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