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A Neuro-Fuzzy Based System for the Classification of Cells as Cancerous or Non-Cancerous

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ABSTRACT

Objectives: *In this study, we developed a neuro-fuzzy based system for classification of cancerous and non-cancerous lung cells.* ***Methods:*** *Images were pre-processed using median filter algorithm, segmented using marker-controlled watershed algorithm, and were extracted using gray-level co-occurrence matrix. A hybridized diagnosis system that made use of neural network and fuzzy logic for classification of lung cells into cancerous and non-cancerous cells is modelled. Computed tomography (CT) scan image dataset of the lung was downloaded from The Cancer Imaging Archive dataset. Neural network performed the training and classification of the lung cells with back-propagation algorithm, while the cancerous cells were passed into fuzzy inference system to determine the lung cancer stage.* ***Results:*** *Our system was able to successfully classify the imported CT scan images into normal or abnormal with considerably high accuracy of 70% and precision of 89%. This system can support physicians in decision making when diagnosing cancer.*

Keywords: Neuro-fuzzy, Cancerous cells, Non-cancerous, Classifications, Grey level

INTRODUCTION

Cancer is considered to be amongst the most severe diseases in the world with a very high mortality rate [1,2]. It occurs as a result of irregular changes in the genes accountable for regulating the growth of cells. Cancer occurs in different forms in human; this may include colon cancer, breast cancer, lung cancer, etc. [3]. Of these, lung cancer is arguably the deadliest resulting from abnormal reproduction of cells in the lung [4]. Lung cancer has caused more deaths in both men and women than any other disease [5]. Identification of lung cancer at its early stage is paramount for successful treatment and can increase the chance of patient's survival [4,6]. Several scientific interventions have leveraged on information and communication technology (ICT) to improve early identification. These responses are referred to as e-health. Automated diagnostic systems leveraging artificial intelligence (AI) are an important and vital aspect of e-health that has elicited numerous research interventions with the attendant results ultimately changing the way diagnosis are handled. Automated diagnosis systems and medical image processing assist doctors in the understanding of medical images such as computer tomography (CT) scan, X-ray, magnetic resonance imaging (MRI) and ultrasound diagnostics in a more efficient manner. It helps in analyzing and evaluating image data comprehensively thereby decreasing the traditional approach of interpreting the images. The use of AI in scheduling or constructing modified medical system is essential regarding precision and accuracy in diagnosing disease and treatment [7].

In recent years, diagnosis systems powered by machine learning tools have been deployed to assist medical personnel in analyzing medical images such as CT image, X-ray and MRI and detecting the occurrence of lung cancer with considerable success. One such tool which has enjoyed considerably large amount of research interests due to its intuitive abilities and advanced computational features is the artificial neural networks (ANN). However, the neural network is only proficient in learning and classification of lung cells into normal and abnormal (cancer) without stating precisely the degree at which the cells are affected. Fuzzy logic, on the other hand, is proficient in specifying the extent of disease although it is not sufficiently expert in learning and generalizing [8]. To overcome the individual limitations of these techniques, we hybridized neural network and fuzzy logic to achieve high performance both in classifying and determining the stage of the cancer.

In this paper, we report a neuro-fuzzy based system which we deployed for the classification of cells as cancerous or non-cancerous. We used gray-level co-occurrence matrix (GLCM) for feature extraction.

E-health

The deployment of ICT techniques and infrastructure in the administering of health services is broadly referred to as 'e-health.' ICT is often deployed for the purpose of enhancing the provision of health care. This use of ICT for health purpose may span application areas such as diagnosis, treatment, health related researches, education, tracking diseases, and monitoring public health. Automated diagnostic systems utilizing AI is a critical and imperative part of e-health. It enhances the efforts of medical personnel to be more productive and less cumbersome. Intelligent systems, especially, artificial neural networks (ANN) and fuzzy inference systems (FIS) have been used in planning or building modified medicinal framework with emphasis on exactness and precision in diagnosing infection and treatment. Other AI techniques often deployed may include Bayesian systems, support vector machine (SVM).

Artificial Neural Networks

Artificial neural networks (ANN) is an algorithmic mimicry of the human neural system to process complex, non-linear information structures and discover pattern for learning and arrangement of data. ANN are systems whose computational models are motivated by the human brain and capable of learning and pattern recognition using training and testing phase [5,9,10]. The internal architecture of the neural network is equipped to cater for a variety of issues identified with image processing like feature extraction, image segmentation, pattern recognition, image compression, and image classification.

Work on neural networks was inspired from the beginning by the understanding of the complex computational workings of the human brain which differs from what is obtained from the digital computer. There are at least 100 billion of interconnected elements of the human brain; these elements, known as neurons are tools that read and process sensory input data in the human senses [11-13]. The neurons comprise of three major components: the dendrites, the cell body, and the axon. The dendrites transmit electrical signals into the cell body, these signals are then processed by the cell body based on set thresholds and are then transmitted to other neurons by the axon [12,14]. The point of contact between an axon of one cell and a dendrite of another cell is called a synapse. Ultimately, the synapse is responsible for transmitting and receiving all impulses from the senses. These impulses are encoded as electrical signals and processed based on a set threshold [9]. Figure 1 shows a simplified schematic diagram of two biological neurons.

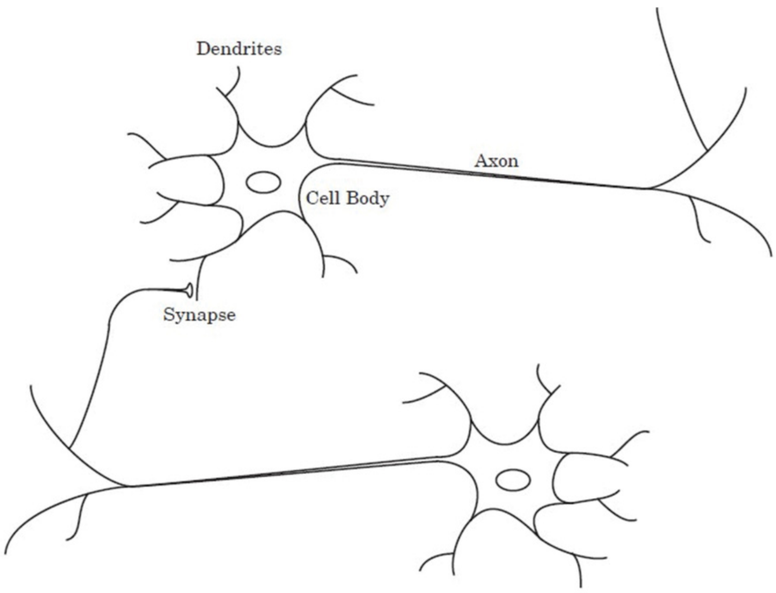

Figure 1 Schematic drawing of biological neurons [12]

The Neuron Model

Motivated by the human neural system, reference [15] proposed a model neuron to mimic the neural system's ability to transmit and receive information processes. This model later became a prototype in the development of subsequent ANN models. A neuron is a data processing unit which is central to the function and operation of the neural network. In Figure 2, we show the generic mathematical model of neurons in the ANN model.

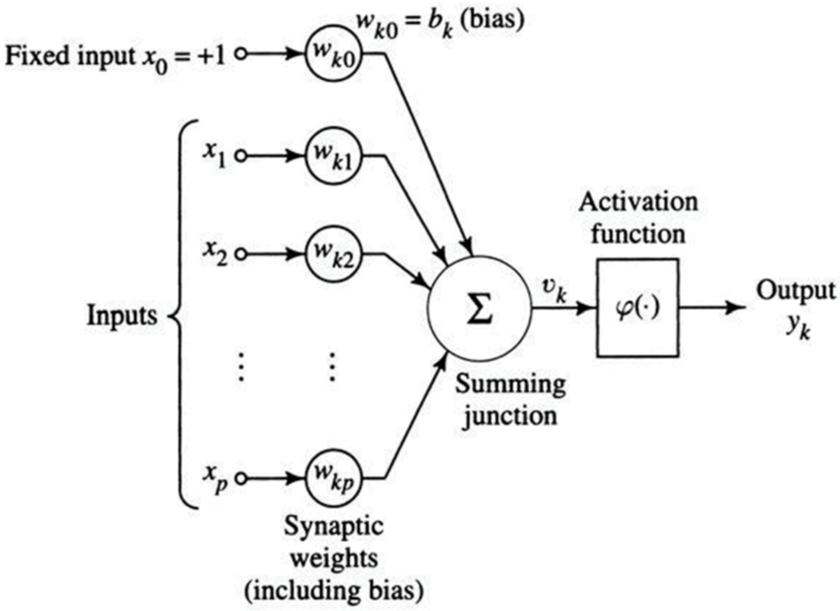

Figure 2 Non-linear model of a neuron [10]

We may identify three essential elements of the neuron model:

I. A set of synapses characterized by weight which is the strength of the neuron. The weight is positive if the supplementary synapse is excitatory, negative if the synapse is inhibitory.

II. An adder function for including the input signals, weighted by the comparing synapses of the neuron.

III. An activation function used in restraining the amplitude of the output neuron. The commonly used normalized range for amplitude of yield of a neuron is composed as the closed unit interim [0, 1] or [-1,1].

Using mathematical expressions, we may define a neuron k by writing the following pair of equations:

$$u_k = \sum_{(j=1)}^{n} w_{kj} x_j \tag{1}$$

$$y_k = \varphi(u_{(k)}) + b_{(k)} \tag{2}$$

u_k is the output of the adder function neuron model;

x_j is data or input signal on path synapse *j*;

w_{kj} is the weighted in the path of synapse *j* to *k* neuron;

y_k is the output of the neuron dependent on the activation function $\varphi(u_k)$ and bias $b_{(k)}$.

There are a number of prominent conventional ANN algorithms in literature which include back-propagation, single layer perceptron, Kohonen self-organizing networks [13]. The back-propagation (BP) training algorithm appears to be the stand-out of them all. One study showed that BP is by far faster than several ANN learning approaches [16]. BP is actualized by the application of the sigmoid function which gives additional vital data to the system. Back-propagation function is computed by finding the squared error of the whole network and afterward figuring the error period for each of the output and hidden units; this is done by accepting the output from the past neuron layer as input. The weights of the whole network are adjusted in dependence on the error term and the given learning rate. Another study observed that BP algorithm could be broken to four principal steps which are [17]:

i. Feed-forward computation

ii. Back propagation to the hidden layer

iii. Back propagation to the output layer

iv. Weight updates

Back-propagation networks involve three layers of units which are input layer, hidden layer, and output layer. The output from the input layer connects the hidden layer through a node. Likewise, the output from the hidden layer also maps to the output layer to deliver the final output of the ANN. In a back-propagation neural network, the network propagates the input pattern from layer to layer until the output pattern is created by the output layer. If the actual patterns differ from the target output patterns, the weights are retuned to reduce this error, and then propagated backward through the network from the output layer to the input layer [18]. The algorithm is stopped when the value of the error function has become sufficiently small.

Fuzzy Logic

The fuzzy logic model was first conceptualized by L.A. Zadeh in his landmark paper in 1965 [19], although it took another nine years for it to become widely accepted through the pioneer work of E. H. Mamdani in the implementation of an automatic steam engine [20].

The fuzzy system is unique because it has the ability to cater for numerical data and linguistic knowledge concurrently just like the human inference process. It delivers an inference morphology that enables estimated human reasoning competencies to be applied to knowledge-based systems and also offers a mathematical strength to apprehend the uncertainties associated with human intellectual developments, such as thinking and reasoning [21]. In essence, the fuzzy logic paradigm can be summarized as a set of linguistic rules related by the concept of fuzzy implication and compositional rules of inference. The aim is to have a model that can map linguistic control rules from expert knowledge input into an automatic control output [22].

Fuzzy logic can be modelled to interpret the attributes of neural networks and provide more accurate description of their performance [17]. Figure 3 is a graphical depiction of the fuzzy logic system. It is characterized by fuzzy sets and fuzzy if-then rules of the form:

"If x is A then y is B", where A and B are fuzzy sets and x and y are members of the sets.

An FLS consists of four main parts: fuzzifier, rules, inference engine, and defuzzifier.

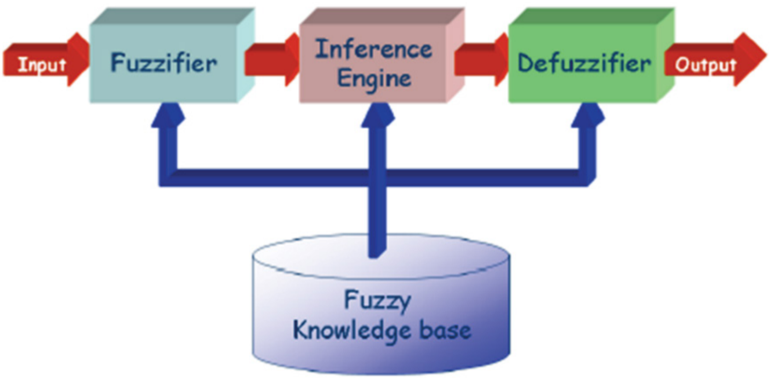

Figure 3 Fuzzy logic system

Fuzzy inference system deploys fuzzy logic to map given input to an output. Fuzzy inference systems are widely used such in control analysis in field of data classification, expert systems, decisions analysis and computer vision 6.

The computation of fuzzy logic can be broken into four algorithmic steps:

The first step involves initialization of the input variables. Secondly, inputted data are converted into a fuzzy set; the process is referred to as fuzzification. The third step involves the inference process based on pre-defined rules. Finally, the output data is defuzzied.

We highlight the algorithmic process as described by [23] below:

- **Step 1: Initialization**

Initialize the linguistic variables and terms

Define the membership functions

Build the rule base (initialization)

- **Step 2: Fuzzification**

Input data are converted to fuzzy values using the defined membership functions

- **Step 3: Inference**

Rules are evaluated by constructing a decision structure involving the combination of membership functions with control rules resulting in fuzzy output.

- **Step 4: Defuzzification**

Resulting fuzzified output is converted into non-fuzzy values

Hybridization of ANN and Fuzzy Logic

The increasing utilization of intelligent hybrid systems in wide ranging application area such as building plan, process control, credit assessment, medical diagnosis, financial trading, and cognitive simulation often are yielding better results. Hybrid systems have the dual capabilities to mitigate weaknesses as well as improve performance of member system. ANN and fuzzy logic systems can be hybridized for this purpose to result in neuro-fuzzy systems.

The integrated inference mechanism in fuzzy logic means it can convert the qualitative feature of the human inference process into processes or values suitable for precise quantitative analysis. Other features of fuzzy logic include learning, fault tolerance, predictive abilities, and parallelism [9]. Its shortfall however, is its lacking structured method for transforming human thought into rule based fuzzy inference system (FIS). Also, the process of adjusting the membership function is time consuming [24]. Consequently, in order to empower the system to manage intellectual vulnerabilities in a way more like people, one may join the idea of fuzzy logic into the neural network. The resulting hybrid system is called neuro-fuzzy.

Review of Related Works

Over the past years, there have been several significant interventions of researches in AI to the enhancement of e-health. Some relevant works are reviewed below:

John proposed a system to classify of brain tumor using wavelet and texture based neural network [25]. It was found that uncontrolled growth of cells in the brain results in death among people. The system processed inputs from T2 weighted magnetic resonance images and classified them into normal, benign, and malignant brain tumors. Wavelet was used for feature extraction to extract the wavelet coefficient from magnetic resonance image (MRI). Texture feature analysis was sectioned into order. In the first order, statistical information was extracted by computing histogram of intensity from the images. In the second order, inter pixel relationships were used to calculate statistical features. Finally, classification was done using probabilistic neural network. This approach yielded results with accuracy of almost 100%.

Ansari and coworkers developed a system for predicting pancreatic ductal adenocarcinoma (PDAC) survival using artificial neural network (ANN) model [26]. A feed-forward ANN was used to construct the survival model; several ANN were combined into a single prediction model. Each multi-layer perceptron was trained using conjugate gradient descent applied to an entropy error function. The system starts with a single node which increments iteratively until the highest performance was found using Harrell concordance index (C-index). The main limitation of this work was the fact that all data were analyzed retrospectively and over a relatively long time frame, with potential changes in imaging, histopathological and treatment approaches over time. In the future, biomarkers such as genes, microRNAs, or proteins can be incorporated into the ANN to increase its predictive ability.

Hassanien proposed a system for diagnosis of MRI breast cancer using multi-layer perceptron neural network

(MLPNN) classifier [27]. The method compared the segmentation using ant-based clustering algorithm against the adaptive ant-based algorithm. A pre-processing algorithm based on fuzzy Type-II was deployed to enhance the quality of the MRI. Segmentation algorithm using the adaptive ant-based segmentation technique was presented to segment breast MRI. Twenty statistical-based features were extracted, normalized, and represented in a database as vector values. Finally, the MLPNN was used as a classifier. Evaluation result showed that adaptive ant-based algorithm demonstrated a better accuracy of 95.1% against 90.70% for ant-based clustering algorithm. MLPNN classification gives an accuracy of 98%.

Similar to earlier work presented by John [25], Al-Amin [28] presented their work using gray level co-occurrence matrix (GLCM) and neural networks to classify cells as either cancerous or non-cancerous. Features such as contrast, correlation, energy, homogeneity were extracted from Image data from National Cancer Institute (NCI) and American Cancer Society (ACS). The corpus was preprocessed to remove noise and then converted to grayscale from RGB. The gray image was then converted to binary image tracing the affected region. Feature extraction used GLCM to extract features. Lastly, ANN was used to classify based on the extracted features. The test with cancerous skin images gave an accuracy of 97.50 and the test with non-cancerous skin images gave an accuracy of 96.67.

Taher, et al. proposed a method for detecting lung cancer at its early stage [4]. Bayesian classification method using histogram analysis was used in pre-processing of image data. Then, mean shift segmentation was applied to segment the nuclei from the cytoplasm. Furthermore, geometric, and chromatic features were extracted from the core region. These features were used in the diagnostic process of the sputum images. Finally, the diagnosis is completed using an ANN and support vector machine (SVM) for classifying the cells. The experimental results establish the efficiency of the SVM classifier over the ANN classifier with 97% sensitivity and accuracy as well as a substantially lesser occurrence of false positives and false negatives. The ANN gave an accuracy and sensitivity of 90% and 94% respectively. Solanki and colleagues also proposed a system for detecting and classifying lung cancer using curvelet transform and neural networks [5]. They used data from VIA/IELCAP public access research database. Their proposed methodology was divided into two parts; first, cancerous cells were detected using curvelet transform. Second, the neural network was used to classify extracted features from the curvelet transform. The result obtained showed an accuracy of 91%. Hamad proposed a system for diagnosing lung cancer using fuzzy logic and neural networks [6]. Some techniques were used to enhance the lung image and segment it to get more information about the characteristic of the CT lung image. Feature extraction was done using GLCM. The GLCM feeds input into the neural networks classifier. The output from the classifier is then supplied as input to the fuzzy inference system to determine the stage of cancer depending on the symptom of the patient. This represents an improvement on [25]. Various image of the lung was used, and the right result has been satisfied.

Methodology

We modelled an Intelligent Diagnosis System using neural network and fuzzy logic. Image datasets were processed and passed into the neural network for training and classification of the lung cells using back-propagation method. The cancerous cells were then passed into fuzzy inference system to determine the lung cancer stage.

Data Collection

Computed Topography (CT) scan image dataset of the lung downloaded from The Cancer Imaging Archive (TCIA) at http://www.cancerimagingarchive.net/. The dataset was used for training and testing of the system.

Features of the System

Our system is divided into two models - the training model and the diagnosis model. In the training model, CT scan images from the dataset undergoes several procedures such as pre-processing, enhancement, segmentation and features extraction. The outputs of these procedures are passed as input training data for the back-propagation neural network. In the diagnosis model, we passed the extracted features obtained from the training model into the neural network for classifier. The classified output is then transferred into the fuzzy system to determine the stage of the cancer.

Image Pre-processing

The imported CT scan dataset undergoes pre-processing in order not just to remove unwanted noise, variation and background information present in the image but also enhance the image quality and present them in an appropriate format. Median filter algorithm was used for the de-noising and smoothing of the image. This algorithm preserves edges and retains details of the image [29].

Segmentation

This process will be carried out on the pre-processed image in order to distinguish more meaningful region and make analysis easier. Segmentation may also depend on a number of features that are enclosed in the image. It may be either color or texture. The image is divided into groups of interconnected pixels that are of similar characteristics such as intensity, shape, and colors. Marker watershed algorithm was used for the segmentation. It separates overlapping objects and marks the important nodule in the image. It is also used to count the number of nodules present and calculate the mean area of the segmented image.

The algorithm steps can be defined as follows,

i. Read the original image

ii. Convert the original image to Grayscale format

iii. Threshold the converted Grayscale image

iv. Morphological reconstruction of the threshold image

v. Find the unknown region (subtract foreground area from background area)

vi. Mark the unknown region (nodule) with markers

vii. Compute the watershed transform of markers

viii. Output the segmented image.

Features Extraction

After extracting the intent regions such as color, shape, size, intensity, it is checked if the extracted regions are nodules or not. The nodules are analyzed to distinguish the true positive regions from the false once. This stage is very important as it extracts significant features to decrease the complexity of image processing and help identify small cancerous nodules. Features extracted in these projects are diameter, perimeter, area, eccentricity, entropy, and intensity.

Neural Network Classifiers

This stage aims at classifying the extracted nodules into cancerous or non-cancerous. The classification aims at predicting certain outcome based on given output. For these to occur, the algorithm processes a training set comprising a set of attributes and the corresponding outcome. The algorithm then tries to identify similarities between the attributes. Finally, the algorithm is then fed with new testing data which contains same set of attributes without the prediction attributes for analysis and prediction.

Fuzzy Logic System

Fuzzy system comprises of three conceptual components: membership function used in the fuzzy rule as rule base which encloses a selection of fuzzy rule, rule base which encloses a selection of fuzzy rule and reasoning mechanism, which computes the inference procedure upon the rules to derive a reasonable conclusion. We deployed the fuzzy system in our work to interpret the output of neural networks and provide precise description of their values.

$$MF = \begin{Bmatrix} T1, if\, 2.5\,cm < T \leq 3\,cm \\ T2, if\, 3\,cm < T \leq 5\,cm \\ T3, if\, 5\,cm < T \leq 7\,cm \\ T4, if\, T > 5\,cm \end{Bmatrix}$$

Linguistic term is defined with the following membership function:

Staging involves assessment of a cancer size and its infiltration into neighboring tissues as well as existence or nonexistence of metastasis in the lymph nodes or other organs. Stage one means that cancer growth is still limited

to the lung. If the cancer is still limited to the lung but close to the lymph, it is stage two. It is stage three if it is within the lung and inside the lymph node. If the cancer has infiltrated other parts of the body, we say it is already in stage four. The system flowchart is shown in Figure 4.

Fuzzy rules

Rule 1: if T1 Then stage I

Rule 2: if T2 Then stage II

Rule 3: if T3 Then stage III

Rule 4: if T4 Then stage IV

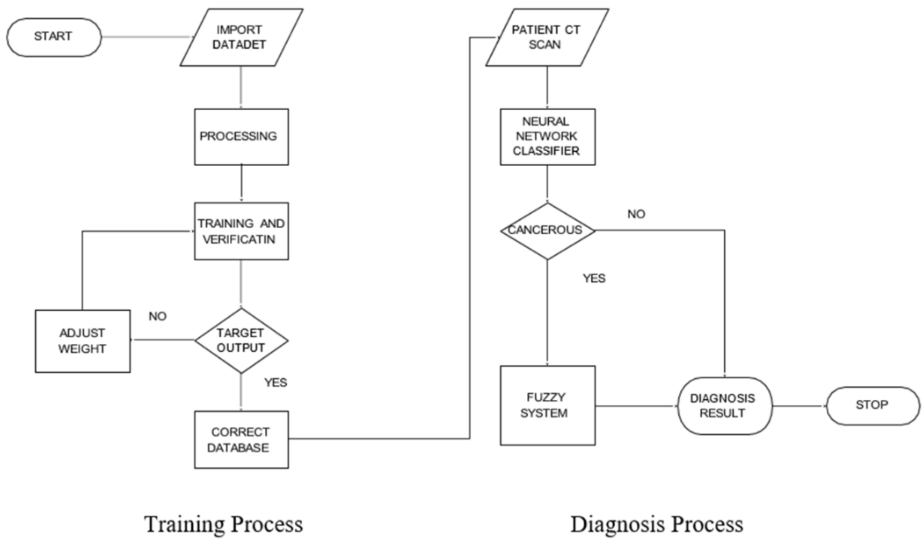

Figure 4 System flowchart

RESULTS AND DISCUSSION

We describe the functional interfaces of the developed neuro-fuzzy based system in this section. The interface as shown in Figure 5 contains menu for performing activities such as importing input Images, pre-processing, feature extraction, and segmentation. Some samples of the imported scans into the developed diagnosis system are shown in Figure 6. The imported CT scan images in Figure 6 have noise. The noise was removed, and the blurred edges improved during preprocessing. Figure 7 shows the pre-processed images.

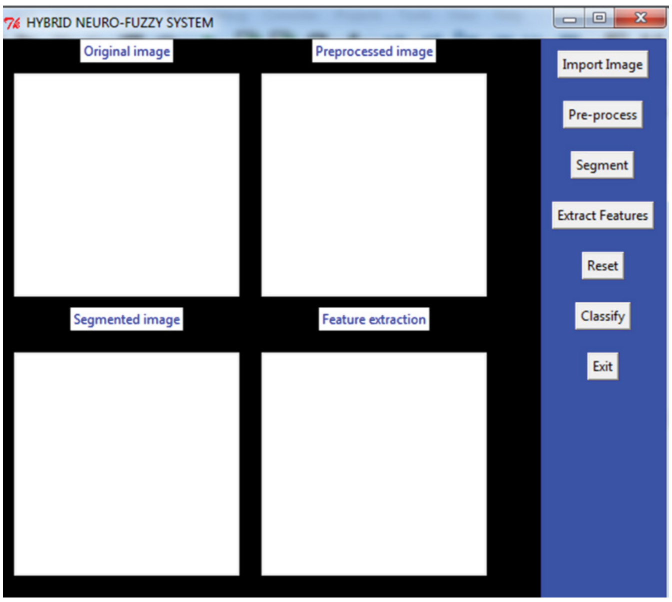

Figure 5 Hybrid neuro-fuzzy system interface

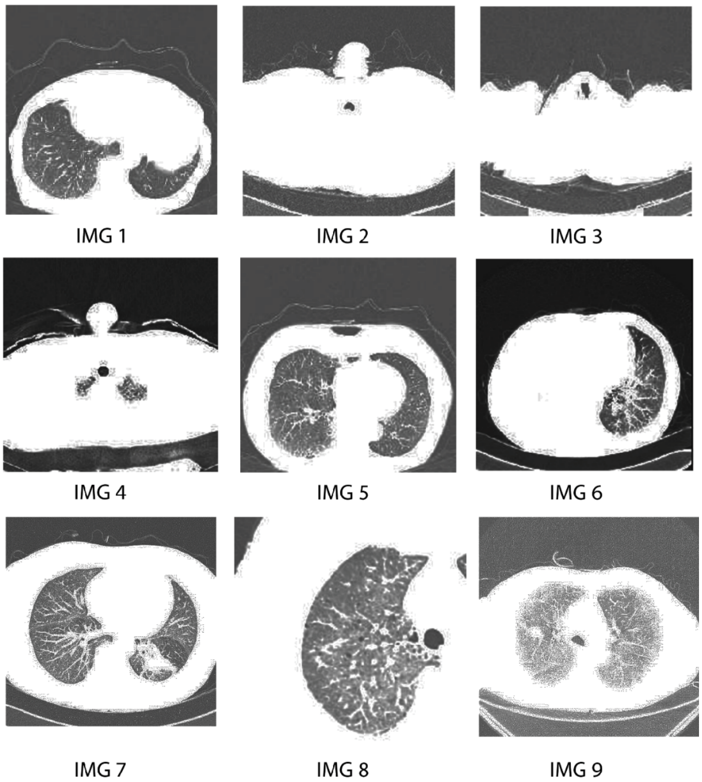

Figure 6 Samples of the original images

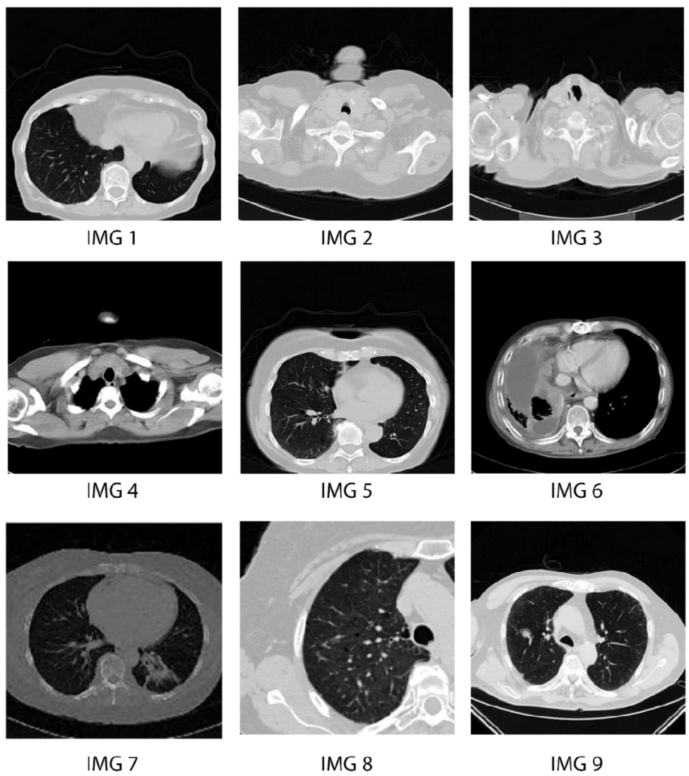

Figure 7 Pre-processed images

Image segmentation was next carried out on the pre-processed images in order to extract positive regions from the image. Some of the segmented images are shown in Figure 8. The white portions in the lung scan denotes positive regions.

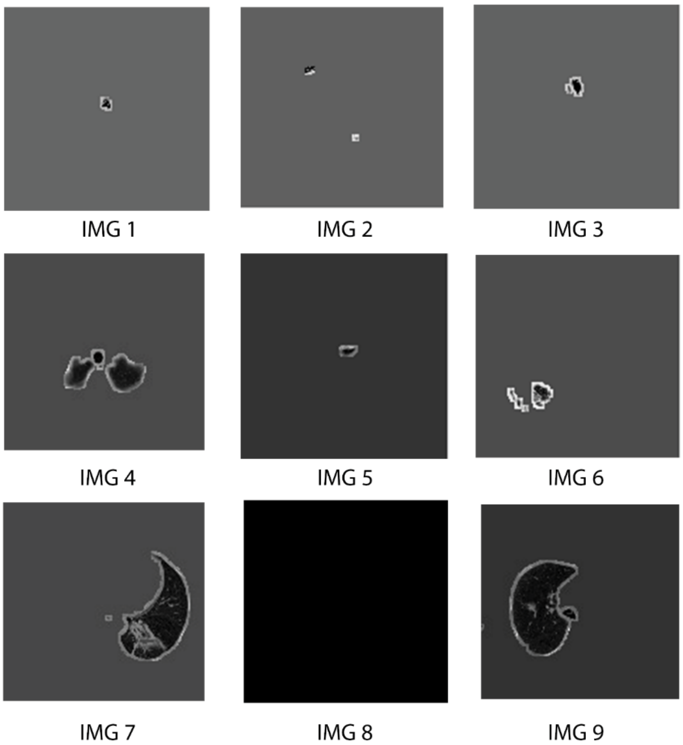

Figure 8 Segmented images

After separating the regions of the lung CT scan into positive and negative regions, the negative regions are discarded keeping the positive regions, feature extraction was carried out. Features such as area, perimeter, eccentricity, and diameter were extracted from the nodule. Results of some of the images features extracted are given in Table 1. The classification results generated from the implemented system are shown in Table 2.

Table 1 Features extracted from images

S/N	Image	Diameter	Perimeter	Entropy	Intensity	Eccentricity
1	IMG1	2.7	598	4.0427	250	0
2	IMG2	3.1	84	4.7536	250	0
3	IMG3	3.7	69	4.1936	250	0
4	IMG4	5.6	64	4.7971	250	0
5	IMG5	3.5	252	4.7755	244.22	0
6	IMG6	6.7	79	4.7747	117.65	0
7	IMG7	7.4	175	4.5695	250	0
8	IMG8	2.2	180	4.7904	224.14	0
9	IMG9	8.2	349	4.7896	248.95	0

Table 2 Classification results for the cancer cells using neuro-fuzzy model

S/N	Image	Neural network classification	Fuzzy result
1	IMG1	ABNORMAL	Stage I
2	IMG2	ABNORMAL	Stage II
3	IMG3	ABNORMAL	Stage II
4	IMG4	ABNORMAL	Stage III
5	IMG5	ABNORMAL	Stage II
6	IMG6	ABNORMAL	Stage III

7	IMG7	ABNORMAL	Stage IV
8	IMG8	NORMAL	None
9	IMG9	ABNORMAL	Stage IV

CONCLUSION

Our classification system was able to successfully classify the imported CT scan images into normal or abnormal following series of operations as stated in the methodology. The images were pre-processed using median filter algorithm, segmented using marker-controlled watershed segmentation and features are extracted using GLCM. This enhanced the performance of our system considerably. In future, the classification performance of several classifiers will also be compared to find the best classifier and implement the hybridized neuro-fuzzy system on an android mobile platform for real time diagnosis.

DECLARATIONS

Conflict of Interest

The authors have disclosed no potential conflicts of interest, financial or otherwise.

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