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Automatic Diagnosis of Diabetic Retinopathy by Hybrid Multilayer Feed Forward Neural Network

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Abtract-- For a particularly long time, Automatic diagnosis of diabetic retinopathy from digital fundus images has been an active research topic in the medical image processing community. This paper describes what is the diagnosis of Diabetic Retinopathy by various image processing techniques and how proposed work can be help to enhace it further. In the beginning section introduction provides the terminology related to DR like fundus images with different types of stages in Diabetic Retinopathy as NPDR(Non Proliferative DR) and PDR(Proliferative DR) levels. Further sections describes different features extraction of Fundus images like exudates, microaneurysms, optic Disc, macula, blood vessels, texture properties like entropy ect. as a responsible parameters for DR with image processing. Brief description of Genetic algorithm and Multilayer feed forward neural network is given. Next section describes how proposed algorithm for classification of Diabetic retinopathy on feature vector can be applicable to train the artificial neural network. This elaborates how Genetic algorithm can be utilized on the training dataset of multilayer feed forward Neural Network . Last section covers the comparing the proposed algorithm with present algorithm to enhance further to expect better results. Finally conclusion on rework and references are included with their reference numbers.

Keywords—Diabetic Retinopathy(DR), Classifier, Pattern Matching, exudates, microaneurysms, optic Disc, macula, blood vessels, NPDR, PDR, sensitivity, specificity, FP(false positives), Genetic algorithm. Optimization, Multilayer feed forward neural network, epochs etc.

I. INTRODUCTION

Diabetes has become one of the rapidly increasing health threats worldwide [21]. Proper and early treatment of diabetes is cost effective since the implications of poor or late treatment are very expensive. Fundus imaging has an important role in diabetes monitoring since occurrences of retinal abnormalities are common and their consequences serious. However, since the eye fundus is sensitive to vascular diseases, fundus imaging is also considered as a candidate for non-invasive screening. The success of this type of screening approach depends on accurate fundus image capture, and especially on accurate and reliable image processing algorithms for detecting the abnormalities. Numerous algorithms have been proposed for fundus image analysis by many research groups [13, 6, 9, 15, 18]. However, it is impossible to judge the accuracy and reliability of the approaches because there exists no commonly accepted and representative fundus image database and evaluation protocol.

In the type 1 diabetes, the insulin production in the pancreas is permanently damaged, whereas in the type 2 diabetes, the person is suffering from increased resistance to insulin. The type 2 diabetes is a familial disease, but also related to limited physical activity and lifestyle [21]. The diabetes may cause abnormalities in the retina (diabetic retinopathy), kidneys (diabetic nephropathy), and nervous system (diabetic neuropathy) [14]. The diabetes is also a major risk factor in cardiovascular diseases [14].

The diabetic retinopathy is a micro vascular complication of diabetes, causing abnormalities in the retina, and in the worst case, blindness. Typically there are no salient symptoms in the early stages of diabetic retinopathy, but the number and severity predominantly increase during the time. The diabetic retinopathy typically begins as small changes in the retinal capillaries. The first detectable abnormalities are mircroaneurysms (Ma) (Fig. 1(a)) which are local distensions of the retinal capillary and which cause intra retinal hemorrhage (H) (Fig. 1(b)) when ruptured. The disease severity is classified as mild non-proliferative diabetic retinopathy when the first apparent microaneurysms appear in the retina [19]. In time, the retinal edema and hard exudates (He) (Fig. 1(c)) are followed by the increased permeability of the capillary walls. The hard exudates are lipid formations leaking from these weakened blood vessels. This state of the retinopathy is called moderate non-proliferative diabetic retinopathy [19]. However, if the above-mentioned abnormalities appear in the central vision area (macula), it is called diabetic maculopathy [21]. As the retinopathy advances, the blood vessels become obstructed which causes micro infarcts in the retina. These micro infarcts are called soft exudates (Se) (Fig. 1(d)). When a significant number of intra retinal hemorrhages, soft exudates, or intra retinal micro-vascular abnormalities are encountered, the state of the retinopathy is defined as severe non-proliferative diabetic retinopathy [19].

The severe non-proliferative diabetic retinopathy can quickly turn into proliferative diabetic retinopathy when extensive lack of oxygen causes the development of new fragile vessels [19]. This is called as neo-vascularisation (Fig. 1(e)) which is a serious eye sight threatening state. The proliferative diabetic retinopathy may cause sudden loss in visual acuity or even a permanent blindness due to vitreous hemorrhage or tractional detachment of the central retina. After diagnosis of diabetic retinopathy, regular monitoring is needed due to the progressive nature of the disease. However, broad screenings cannot be performed due to the fact that the fundus image examination requires attention of medical experts. For the screening, automatic image processing methods must be developed.

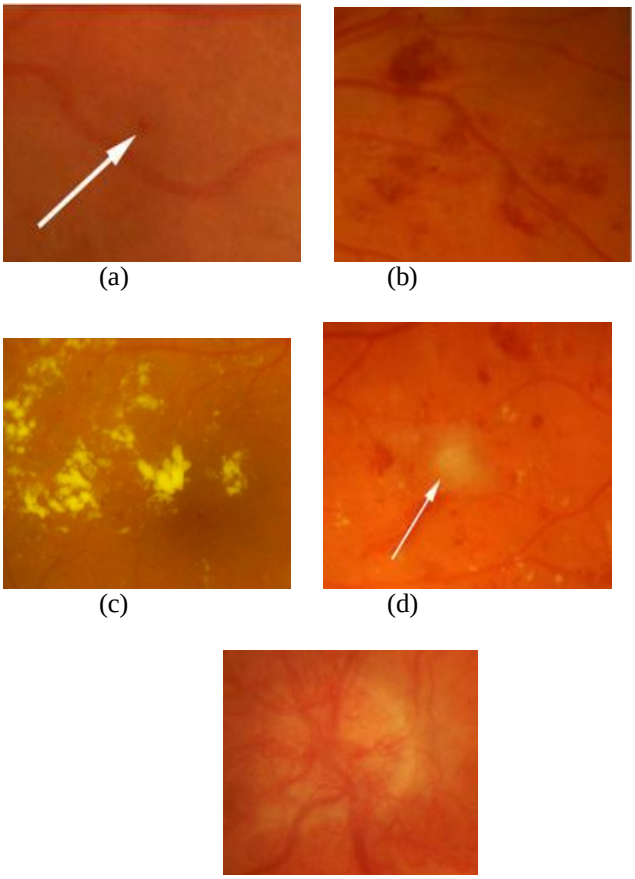


Fig 1: Abnormal findings in the eye fundus caused by the diabetic retinopathy: (a) microaneuryms (marked with an arrow), (b) hemorrhages, (c) hard exudates, (d) soft exudate (marked with an arrow), and (e) neovascularization.

In medical diagnosis, the medical input data is usually classified into two classes, where the disease is either present or absent. The classification accuracy of the diagnosis is assessed using the sensitivity and specificity measures. Following the practises in the medical research, the fundus images related to the diabetic retinopathy are evaluated by using sensitivity and specificity per image basis. Sensitivity is the percentage of abnormal funduses classified as abnormal, and specificity is the percentage of normal fundus classified as normal by the screening. The higher the sensitivity and specificity values, the better the diagnosis. Sensitivity and specificity can be computed as [22]:

$$\text{sensitivity (SN)} = TP/TP + FN,$$
$$\text{specificity (SP)} = TN/TN + FP \quad (1)$$

where *TP* is the number of abnormal fundus images found as abnormal, *T N* is the number of normal fundus images found as normal, *FP* is the number of normal fundus images found as abnormal (false positives) and *FN* is the number of abnormal fundus images found as normal (false negatives). Sensitivity and specificity are also referred to as the true positive rate (TPR) and true negative rate (TNR), respectively. As mentioned previously, the diagnosis of diabetic retinopathy can be divided into the following two categories:

1. Screening of the diabetic retinopathy
2. Monitoring of the diabetic retinopathy

Most automatic systems approach the detection directly using shape, color, and domain knowledge of diabetic retinopathy findings, but the abnormalities can also be found indirectly by detecting changes between two fundus images taken from the same eye in different time moment [11, 17]. The direct approach contributes to screening of the disease, where indirect approach contributes to both screening and monitoring of the diabetic retinopathy. Both approaches use roughly the following stages for finding abnormalities in fundus images: 1) image enhancement 2) candidate diabetic retinopathy finding detection 3) classification to correct diabetic retinopathy category (or hypothesis rejection).

The automatic methods either use the vital domain information provided by the normal fundus parts or remove them due to their similar color and shape appearance with abnormal fundus findings.

II. PROPOSED ALGORITHM

Proposed algorithm for the Classification of DR is given as below in *fig 2.1*

Step 1. Input Fundus Image
Step 2. Various Feature Extraction by applying image processing Tools.
Step 3. Creation of feature vector of input image
Step 4.Classification with HybridMLFFNN

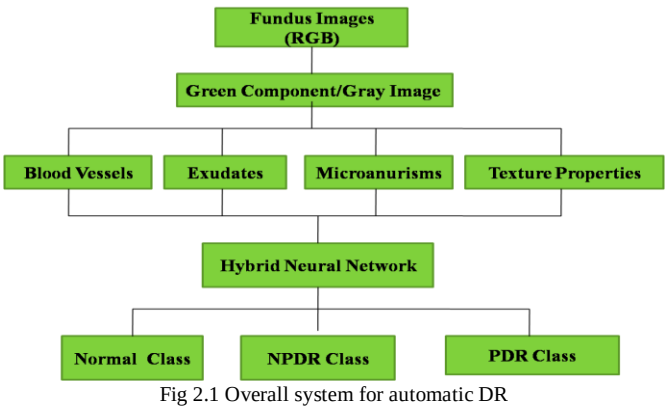


Fig 2.1 Overall system for automatic DR

III. FEATURE EXTRACTION

Fundus images from Fundus camera is the input for feature extraction module. Extracted features are Microaneurysms, Exudates, Blood vessels and Texture properties.

A. Blood Vessels Detection

Blood vessels are extracted in this project for the identification of diabetic retinopathy. The contrast of the fundus image tends to be bright in the centre and diminish at the side, hence preprocessing is essential to minimize this effect and have a more uniform image. After which, the green channel of the image is applied with morphological image processing to remove the optical disk. Image segmentation is then performed to adjust the contrast intensity and small pixels considered to be noise are removed.

Another green channel image is processed with image segmentation and combined with the mask layer. These two images are compared and the differences are removed. The obtained image would represent the blood vessels of the original image.

Output of the Blood Vessels is as in *fig 3.1*

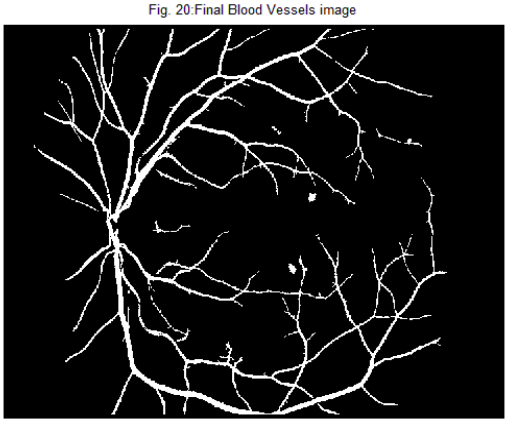


Fig 3.1 Blood Vessels

B. Exudates Detection

Exudates appeared as bright yellow-white deposits on the retina due to the leakage of blood from abnormal vessels. Their shape and size will vary with the different retinopathy stages. The grayscale image is first preprocessed for uniformity before the morphological image processing is applied to remove the blood vessels and identify the exudates region. The exudates are detected after removing the border, optical disk and non-exudates area.

Output of the Exudates is as in *fig 3.2*

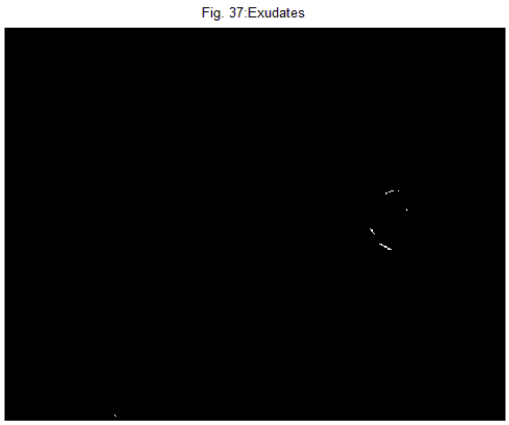


Fig 3.2 Exudates

C. Microaneurysms Detection

Microaneurysms appeared as small dark round dots (~15 to 60microns in diameter) on the fundus images. They are small bulges developed from the weak blood vessels and are the earliest clinical sign of diabetic retinopathy [9]. Hence, it is essential to detect them during the mild stage. The number of microaneurysms would increase with the stage of the retinopathy. The grayscale image is used to detect the circular border and optical disk mask. The green channel of the image first finds the edges using canny method before removing the circular border to fill the enclosed small area. The larger areas are then removed and applied with AND logic to remove the exudates. The blood vessels and optical disk are then removed to obtain the microaneurysms.

Output of the Microaneurysms is as in *fig 3.3*

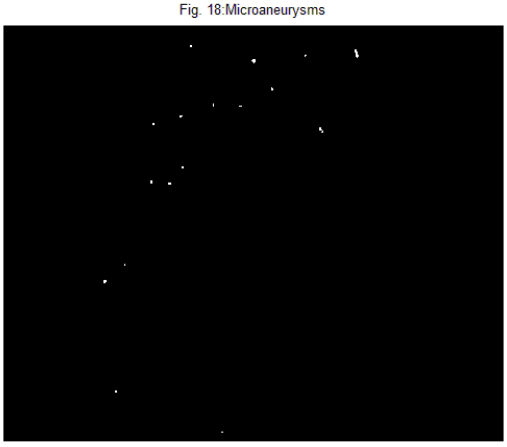


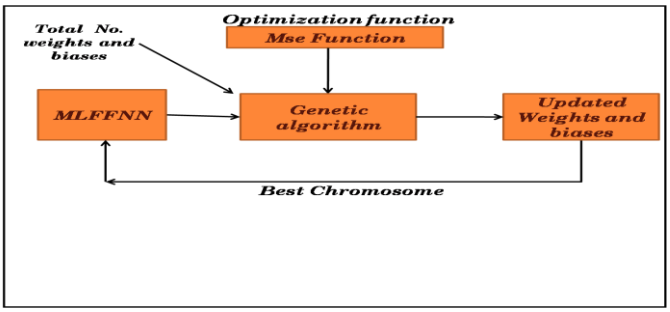
Fig 3.3 Microaneurysm

After applying the module 1 we get the extracted feature areas. The results of few images is given in following table

Blood Vessel	Exudates	Microanurysms	Entropy	Homogenei
30550	90	216	7.6165	0.9885
34974	383	259	7.763	0.9875
28100	306	640	7.6666	0.989
32923	0	41	7.5356	0.993
30634	412	393	7.6356	0.9918
41719	0	300	7.6531	0.9915
51522	90	514	7.7541	0.9884
22379	52	261	7.4883	0.9897
35583	0	65	7.5232	0.9902
37239	6	35	7.5469	0.9908
28683	270	672	7.564	0.9896
27795	12	232	7.5089	0.9877
47040	110	498	7.7524	0.9884
49904	213	507	7.6839	0.9861
41103	0	54	7.6173	0.9893
48427	0	175	7.6403	0.9896
35798	0	84	7.581	0.9907
38192	0	99	7.631	0.9897
30271	0	19	7.5855	0.9919
42984	0	131	7.6291	0.9929

IV. DESIGN & IMPLEMENTATION OF PROPOSED MECHANISM

How the data from the features extractions are being fed into the Hybrid Neural Network (HMLFFNN) for training and how the test is conducted. The result of the test data and the accuracy of the classifier are also being discussed. The block diagram shown below the design of Hybridization. In this the Mean square error (MSE) of the feed forward is as optimization function of Genetic Algorithm. The Weight and Bias of the neural Network is as the Number of Variables for the Genetic algorithm as Chromosome.



V. CLASSIFICATION USING HYBRIDMLFFNN

The MLFFNN is a multilayer feed-forward back propagation neural network as in *fig 4.1* and uses supervised learning to train the neural network. Supervised learning is by providing the ANN with input data and matches them with output results. Its weights would adjust according to its learning rules as it undergoes training before being tested for accuracy. The architecture MLFFNN used for classification in this project as shown in the figure below.

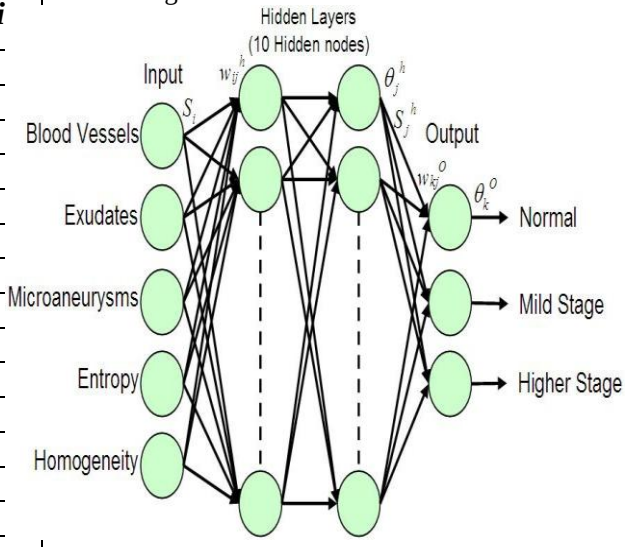


Fig 4.1 Four-layer feed-forward neural network classifier

The input layer is made up of nodes to accept the 5 data values while the subsequent layers process the values using activation function. There are 10 neurons for each "hidden layer" and the trained network would output binary numbers which represent the different stages.

VI. TRAINING DATA SET AND TESTING DATA SET

The values of all the subjects are input into to ANOVA test the hypotheses between the groups as mean and standard Deviation(SD). Extracted features are Normalized before feeding it to the NN between 0 to 1. The Normalization is done with matlab function and arranged in excel sheet for Dataset creation.

Part of Training data(matfile1) for HybridMLFFNN

0.0055607	0.0204499	0.97805372	0.97032636	0.831926	0	1;
0.09947482	0.26278119	0.98135003	0.96305752	0.643454	1	0;
0	0.1799591	0.98444742	0.94459168	0.624104	0	0;
0.00030893	0	0.97632432	0.9575895	0.545847	0	1;
0.06703738	0.83128834	0.97632432	0.97101544	0.934866	1	0;
0	0	0.99047297	0.98797252	0.572079	0	0;

The data as shown above is a portion of the data from matfile1 being fed into the ANN for training The goal of the training is 0.001 which means the allowed error is targeted to be less than 0.1%. No. of Epoches considerd as 5000. After executing the Genetic algorithm solver in Matlab by providing the mse_test function as a fitness function and weight and biases of neural network as an Number of Variable as a parameters the GA gives the output. The output of GA is arranged in table format as shown in below. Total 50 Generations are run and the result of each generation is shown in the table below. In every generation f-count is the total count of the Mse Test function

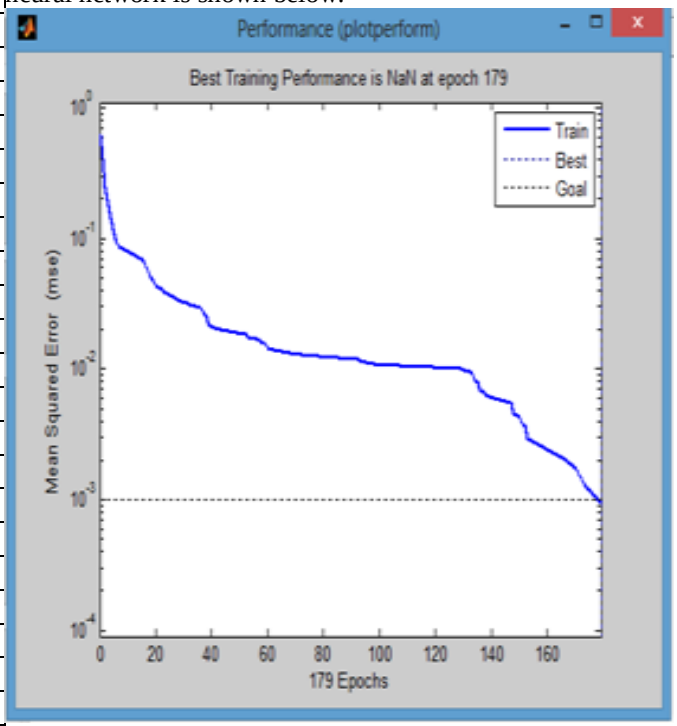
and is cumulative with all generation. Best f(x) is the best value of fitness function among all f-count. Mean f(x) is the mean value of the Fittness function so its mean fitteness value. So in 51st generation it gives us the one of the optimized value which is finally used as base value for the NN.

Generation	f-count	Best f(x)	Mean f(x)	Stall Generations
1	20	1.68E-05	0.04077	0
2	40	1.68E-05	0.03653	1
3	60	1.68E-05	0.02288	2
4	80	1.68E-05	0.02772	3
5	100	1.68E-05	0.0242	4
6	120	1.68E-05	0.01681	5
7	140	1.68E-05	0.01394	6
8	160	9.38E-08	0.01614	0
9	180	9.38E-08	0.01478	1
10	200	9.38E-08	0.01775	2
11	220	9.38E-08	0.01237	3
12	240	9.38E-08	0.0196	4
13	260	9.38E-08	0.01926	5
14	280	9.38E-08	0.0122	6
15	300	9.38E-08	0.01837	7
16	320	1.95E-09	0.02191	0
17	340	1.95E-09	0.01403	1
18	360	1.95E-09	0.01876	2
19	380	1.95E-09	0.01414	3
20	400	1.95E-09	0.01416	4
21	420	1.95E-09	0.007473	5
22	440	1.95E-09	0.0227	6
23	460	1.95E-09	0.01427	7
24	480	1.95E-09	0.02348	8
25	500	1.95E-09	0.01482	9
26	520	1.95E-09	0.01418	10
27	540	1.10E-09	0.01575	0
28	560	1.10E-09	0.01376	1
29	580	1.10E-09	0.0133	2
30	600	1.10E-09	0.01057	3
31	620	1.10E-09	0.01831	4
32	640	1.10E-09	0.01513	5
33	660	1.10E-09	0.01551	6
34	680	1.10E-09	0.01599	7
35	700	1.10E-09	0.01806	8
36	720	1.10E-09	0.01153	9
37	740	1.10E-09	0.01584	10
38	760	1.10E-09	0.02014	11
39	780	1.10E-09	0.01424	12
40	800	1.10E-09	0.01467	13
41	820	1.10E-09	0.01829	14
42	840	1.10E-09	0.01845	15
43	860	1.10E-09	0.01786	16
44	880	1.10E-09	0.01454	17
45	900	1.10E-09	0.006824	18
46	920	1.10E-09	0.01539	19
47	940	1.10E-09	0.007176	20
48	960	1.10E-09	0.01014	21
49	980	1.10E-09	0.01689	22
50	1000	1.10E-09	0.01997	23
51	1020	1.10E-09	0.01945	24

A. Multi Layer Feed Forward NN in matlab:

Y = newff (P,[10, 10, 2] , {‘tansig’,’tansig’,’purelin’} , ’traingdm’);

Where, P is vector with min max values for all the inputs, Second parameter is size of neural network layers, Third parameter transformation function. Performance Plot of the neural network is shown below.



B. Part of Testing Data

0.4579	0	0.8937	0.9616	0.9934;
0.4779	0.0278	0.2209	0.9646	0.9895;
0.5471	0.1183	0.2648	0.9832	0.9885;
0.4395	0.0945	0.6544	0.971	0.99;
0.4792	0.1273	0.4018	0.967	0.9928;
0.3501	0.0161	0.2669	0.9484	0.9907;
0.5566	0	0.0665	0.9528	0.9912;
0.4487	0.0834	0.6871	0.958	0.9906;
0.4348	0.0037	0.2372	0.951	0.9887;
0.6429	0	0.0552	0.9647	0.9903;
0.7575	0	0.1789	0.9676	0.9906;

0.56	0	0.0859	0.9601	0.9917;
0.5974	0	0.1012	0.9665	0.9907;
0.4735	0	0.0194	0.9607	0.9929;
0.5048	0.088	0.0941	0.962	0.9932;

The data as shown above is a portion of the data from matfile2 being fed into the ANN for Testing. The above is extracted features from the feature extraction module.

C. Output and Results

- 00- Normal eye ,
- 01- Mild DR stage,
- 10 or 11- Severe DR stage

After Testing Four Layer Feed Forward Neural Network.
Output is shown for only 13 images
y =

Columns 1 through 8
0.9872 -0.0672 0.9892 0.9884 0.4841 0.9749 0.7267 0.9892
0.0692 0.9527 -0.0052 0.0183 -0.9939 -0.1926 0.8554 -0.0036

Columns 9 through 13

0.5343 0.9899 0.9875 0.9889 -0.0464

-0.9304 -0.1752 0.0536 0.0087 0.9944

x =

1 0 1 1 0 1 1 1 1 1 1 1 0

0 1 0 0 1 0 1 0 1 0 0 0 1

D.Sensitivity

The table as shown below is the breakdown of the accuracy of the classifier. Sensitivity refers to the probability of a positive test among the subjects with the condition while Specificity refers to the probability of a negative test among the subjects without the condition. The equation is as follows
Sensitivity = TP/TP+TN

No. Of Test	Truly Classified TP	Wrongly Classified TN	Sensitivity (%)
24	20	4	0.83333

VII. Future Work

Biomedical image processing requires an integrated knowledge in mathematics, statistics, programming and biology. Based on the results of the classifier, this project has a sensitivity of approximately 80%-85% for various observations. It is able to achieve a fairly accurate classification for mild and higher stages but not for normal class resulting in a possible high false alarm.

This might be improved by fine tuning the threshold values used on the images and more images could be used to improve the overall system. For this project, I had learnt various techniques of image processing and was able to extract the features, namely blood vessels, exudates, microaneurysms and texture properties (homogeneity and entropy) from the fundus images. I was able optimize the Weight and biases of MLFFNN by using GA tool in matlab. In this MSE is considered as optimization function for GA and I am able to take it as fitness function for weight and biases. Total weight and biases are as number of variables for the GA. Training of by back propagation to perform classification with the hybridization with GA is satisfied me. I was also able to design a GUI to perform classification on the images automatically.

During Hybridization we must take of proper assignment of GA parameters so that GA will give better results. Training DataSet has 45-50 samples and Testing Dataset has 24 samples. After testing TP=20 and TN=4, Specificity is found that 0.8333.

From this work , there are areas that can be improved to raise the overall accuracy or enhance the system. The followings are some of the recommendations for future work to achieve this. We can further fine-tune the threshold values used for image processing. There is scope to explore other features that could be added for classification. Hybridization can be fine tune by applying various Genetic algorithm features. Hybridization level can be increased by adding some other technology like fuzzy logics. Optimization may be done with some different parameters of NN.

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