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Risk Level Prediction of Diabetic Retinopathy Using Adaptive Neural Fuzzy Inference System

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Abstract

Diabetes is common now a days and almost everyone had its awareness. There are many ways to control it through various precautionary protocols like life style maintenance of eating habits/physical exercise/stress relief procedures/yoga/avoiding alcoholic and tobacco habits etc, along with proper medication, approximately one in ten adult people worldwide suffer from diabetes. The chronic condition of diabetes affects the human organs like eyes, the brain, the heart, the kidney, and the foot. The most common cause of visual impairment which affects about twenty five thousand patients is diabetic retinopathy. Adaptive neuro fuzzy system is used to create a rule base for fuzzy system. The fuzzy system is then used to find out the risk level of the diabetic retinopathy that the patient has. The dataset was taken from Diabetic Retinopathy Study (DRS). The accuracy, specificity and sensitivity found in this study were 92.9%, 71.4% and 97% respectively. The developed system will be a great use to help patients, doctors and many health practitioners in saving time and cost compared to conventional methods.

Keywords: *Diabetic Retinopathy, ANFIS, MATLAB, Sugeno*

1. Introduction

During Diabetic Retinopathy is a diabetic complication which damages the retina of eye due to high blood sugar level. Diabetic Retinopathy has to be treated and managed else it will lead to blindness. Diabetic retinopathy is leading cause of visual impairment in USA. According to CDC (Center for Disease Control and Prevention), between twelve thousand and twenty-five thousand new cases occur in United States of America from diabetic retinopathy. And many of these cases can be prevented with proper monitoring and intervention at the right time. Blood vessels help in supplying a constant flow of blood to retina. The blood vessels in retina are affected because of diabetic condition. Retina is a layer which is present at the back of eye which converts light into electrical signals and then turns them into images. The high level of sugar in blood damages the blood vessels which provide oxygen to retina. And this leads to blood leak which causes blurring of vision, hemorrhage and ultimately retinal detachment. The condition develops slowly with first stage named background retinopathy, in which the vision is not affected but tiny bulges are developed in the blood vessels. Frequent monitoring of eyes is the only treatment for the first stage of disease. The next stage has more severe blood leakage which is known as pre-proliferative retinopathy. The final stage where new weak vessel grows and these bleed easily. After this the leakage from blood vessels enter in eye's vitreous which can cause serious vision problems and lead to complete visual impairment. The stage results in some loss of vision and is known as proliferative

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retinopathy. In the advanced stage of disease treatment is to seal the blood vessels with the help of laser.

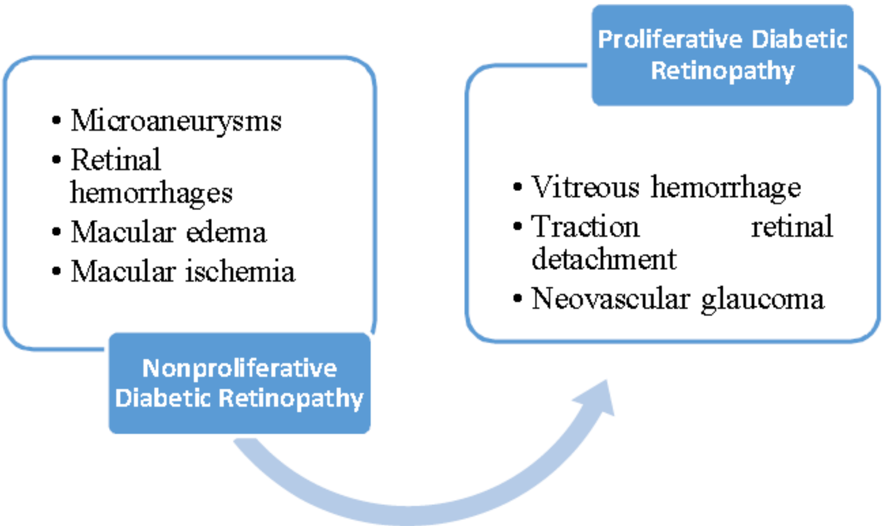

Figure 1. Diabetic Retinopathy Stages

According to experts, people with higher blood pressure, who have diabetes for long time, pregnant women, people having high cholesterol and people having Asian or Afro-Caribbean background are at greater risk for diabetic retinopathy. Early detection along with laser treatment has proved its great effectiveness in removing the condition Avastin (bevacizumab), Lucentis (ranibizumab), and Eylea (aflibercept) are anti VEFG drugs used by US for the treatment of diabetic retinopathy. Focal/grid macular laser surgeries are used for curing the disease if anti VEFG drugs do not show any improvement in curing the disease. To reduce the swelling Laser are used. Blood vessels which highly damage the retina are reduced using panretinal photocoagulation surgery.

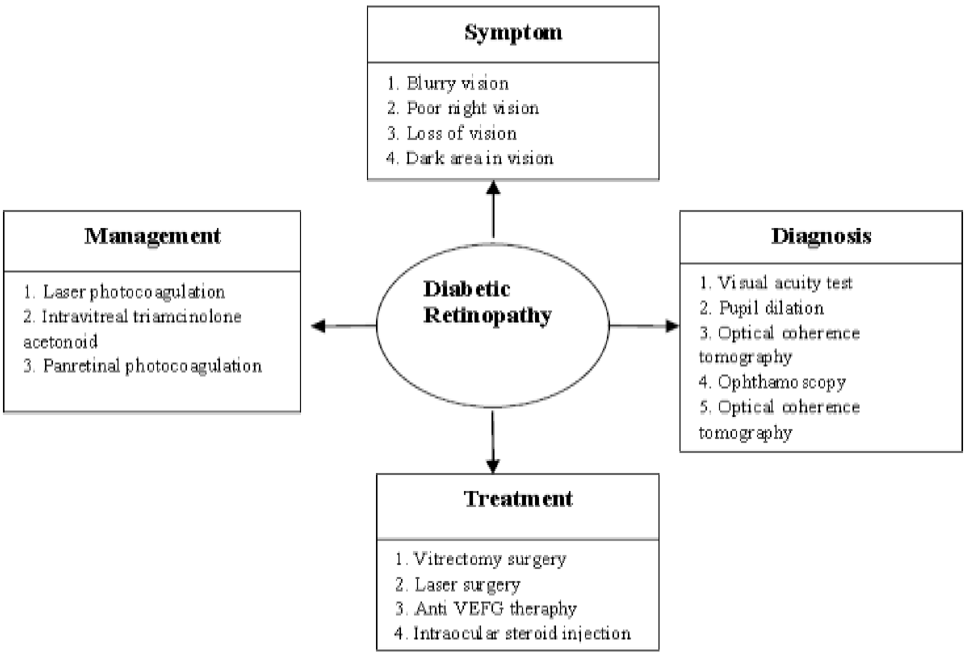

Figure 2. DR symptoms, Diagnosis and Treatment

In India 6 Million people are affected by Diabetic Retinopathy and it is estimated that it will increase to 10 Million by 2035.By 2030, Diabetic Retinopathy will increase by 69% in developing countries and 20% in Industrialized countries. In which type1 diabetics affected by diabetic retinopathy are 50% and type 2 are 30%. There are about 93 Million people being affected by diabetic retinopathy globally in which 17 Million are Proliferative type, 21 Million are Macula oedema. 1.85 Million Globally lost their vision because of diabetic retinopathy. Worldwide prevalence statistics of diabetic retinopathy is given in the following table country wise. Diabetic type's statistics are also added in the table. Global Prevalence of Diabetic Retinopathy prevalence is 35.36% in 2012 with Type1 prevalence percentage is 77.31% and Type - 25.16%. This percentage would increase as the number of diabetic patients increase.

Diabetic Retinopathy Statistics			
Global Prevalence of Diabetic Retinopathy 35.36% in 2012 Type1 - 77.31% Type - 25.16%			
Country/Yr	Overall Prevalence percentage	Type1 diabetic Prevalence percentage	Type1 diabetic Prevalence percentage
United Kingdom/2015	32.4	5.00	30.3
Spain/2010	26.7	36.5	26.1
Norway/2013	26.8	78.0	25.0
South Africa/2013	25.8	36.9	21.4
Australia/2014	26.3	26.3	26.3
Tunisia/2014	35.9	35.9	35.9
Russia/2009	45.9	54.6	34.6

Worldwide Diabetic Retinopathy Prevalence Percentage		
Year	Country	Prevalence percentage
2009	India	18.00
2012	Singapore	30.40
	China	23.00
2013	Bangladesh	21.60
	South Korea	15.80
2014	Nepal	38.26
	Sri Lanka	27.40
	Hong Kong	12.10
	Kenya	35.90

Figure 3. Diabetic Retinopathy Statistics

2. Literature Review

José Tomás, , (2015) [1] developed a web based application which provides user interface to discriminate among patients with and without the presence of diabetic retinopathy by means of an automated digital eye fundus image processing. Blood vessel localization, optic disc localization, bright lesion and red lesion detection are considered for the automated detection. Edge detection is one of the major challenges in the diagnosis of disease. To overcome this challenge Kamil,

Mohammed Y. (2014) [2] proposed a new technique for edge detection based on fuzzy logic which performs better than the traditional techniques. To detect diabetic retinopathy and to calculate its impact on retina Imran, Mohammed, , (2016) [3] presented an automated method which uses diabetic retinopathy's risk factors and the signs of diabetic retinopathy in retina fundus image.

Morphological operations and fuzzy logic was exploited by Basha, S. Saheb, and K. Satya Prasad (2008) [4] for segmentation and identification of diabetic retinopathy from digital fundus images. Morphological operations are used to segment hard exudates, soft exudates and red lesion. Fuzzy logic uses color space values for identifying the presence of DR.

Choudhury, S., , (2016) [5] considered retinal vessel density and exudates for the classification of diabetic retinopathy. Morphological segmentation methods and fuzzy C-means are used for extracting the retinal vessels and exudates. Support vector machine then uses these two inputs for classifying whether the patient is suffering from diabetic retinopathy or not.

Medhi , (2016) [6] presented a method for improving the analysis of diabetic maculopathy which is a sight threatening disease. Diabetic maculopathy affects the vision when the blood starts depositing in the retina. The proposed method involves of two phases. First the fovea is spotted and the region of analysis of maculaopathy is marked. Then spacial fuzzy clustering is employed for the detection of lesion and analysis of disease.

Ayub, Lubna, , (2016) [7] used neural network for the classifying the blood vessels in the retina in to arteries and veins. The ratio of arteriolar diameter to venular diameter called Arteriovenous Ratio is considered to be an important factor for the identification of hypertensive retinopathy. Classification of blood vessels consists of localization of optic disk, segmentation using bottom hat filtering, extraction of statistical and texture features and application of neural networks.

Dhiravidachelvi, E , (2015) [8] proposed a method which determines the types of diabetic retinopathy, its status and suggests the appropriate treatement. Non-Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR) are the types of DR.

Asha , (2015) [9] proposed machine learning techniques for the detection of exudates in retina. The proposed method uses pre-processing, feature extraction and classification. HSI conversion, Local Contrast Enhancement, Histogram Equalization, and Fuzzy C-means segmentation were used for pre-processing the retinal images. Mean, Standard deviation, Centroid and Edge Strength were the features extracted for classification by machine learning techniques. Naive bayes (NB), Multilayer Perceptron (MLP) and Extreme Learning Machine (ELM) were the machine learning techniques proposed.

Vandarkuzhali, T , (2013) [10] developed an automated system for sensing the deviations in the retinal image due to diabetic retinopathy. The proposed automated system uses fuzzy K-means and neural networks for the detection of deviations in fovea. For the detection of new blood vessel in retinal images Saranya, K , (2012) [11] proposed a new method which accomplishes pre-processing, enhancement of the image, segmentation, extraction and classification. Pre-processing is done using Adaptive Histogram Equalization (AHE), enhancement by top-hat and bottom-hat transform, segmentation by fuzzy C-means clustering and classification by K-nearest neighbour classifier. Segmentation plays a major role in image analysis. Selecting a seed pixel is a challenging task in region based segmentation methods. M. Tamilarasi , (2013) [12] proposed Genetic based Fuzzy Seeded Region Growing Segmentation algorithm for selecting multiple seeds which overcomes this challenge.

In renital analysis optic disc is the most significant issue to be considered as this appears as a bright spot in retinal images which be similar to exudates. Hence optic disc has to be removed from retinal images. For the detection of optic disc and exudates Vimala , (2013) [13] proposed an effective and automated method which uses fuzzy C-means clustering for detecting optic disc, K-means clustering for extracting exudates and support vector machine for classification.

Ranamuka , (2013) [14] proposed a new method for the detection of hard exudates. The proposed method uses a mathematical morphology for identifying and eliminating the optic disc and then uses adaptive fuzzy logic algorithm for extracting the hard exudates. Fuzzy set and membership functions are formed using RGB color space in retinal images. To detect the abnormalities in the retinal image and to classify them based on severity T Yamuna , (2013) [15] proposed a new technique. The proposed technique is based on pre-processing, candidate extraction and adaptive neuro fuzzy inference system for classifying the retinal images as normal, mild and severe.

In [22] the author used weighted fuzzy logic to assign weights in training the data to extract sentiments from the labeled tweets and achieved good F-score. where as in [23] the author made a detailed comparison on predictive models and perform analysis on Time series dataset. In [24] the author perform analysis on PIMA diabetes dataset and predicted the levels of diabetes based on insulin feature. where as in [25] the author used gradient ascent algorithm in finding out the exact weights of the terms used in determining the sentiment of tweet and used Boosting approach to improve the accuracy of linear classifier. In [26], the author provides a novel way of performing prediction on Breast cancer dataset, compared the performance of three different feature selection algorithm and proved that genetic algorithm is giving best result in selecting the best feature among all the available feature. SVM algorithms gives the best result in predicting the level of certainty in breast cancer. In [27], the author made an attempt to develop a recommender system, helping in searching the item, that might out found by themselves, in which precision and recall measures are used in measuring the performance of proposed model. In [28], the author made a research in solving the problem in Diabetic Retinopathy. In which, the author proposed a Model, which can capable of calculating the weights, that gives severity level of the patient's eye by using weighted Fuzzy C-means algorithm. In [29], the author proposed a build a model for airlines, that can perform sentiment analysis on customer feedback and achieved Vital accuracy. Where as in [30], the author experimented on finding out the impact of feature selection on overall sentiment analysis and stated that Term frequency have greater impact on analyzing sentiments rather than bigram approach.

3. Methodology

In this paper, we are developing a fuzzy system which approximates the condition of patient based on simple attributes. We used ANFIS toolbox in MATLAB. Results were accuracy, specificity and sensitivity: 0.929, 0.714 and 0.97 respectively. A similar study by Cavalli found the sensitivity of 0.84 and a specificity of 0.64. Earlier studies have shown sensitivity and specificity of 0.839 and 0.727 respectively. Adaptive network dynamically changes the structure of network topology. In case of adaptive neuro systems, the structure of neural network which is underlying is modified according to the modelling data. Fuzzy inference formulated the mapping from input to output using fuzzy logic. This mapping provides a base which allows decision making. Since ANFIS integrates both neural networks and fuzzy logic principles, it captures the benefits of both.

The FIS corresponds to IF-Then rules that have learning capacity to guess nonlinear functions. Hence ANFIS can be considered as a universal estimator. ANFIS is expanded as adaptive neuro fuzzy inference system, or adaptive network based fuzzy inference system. MATLAB provides a toolbox, which allows the function anfis to create fuzzy inference systemFIS whose membership function parameters are adjusted using either a back propagation algorithm or hybrid method. This adjustment helps FIS to learn from the data. These adaptive networks are increasingly becoming popular because of their ability to cope with real world models.

ANFIS is a fuzzy system where membership functions have been turned using neuro-adaptive learning methods similar to those in neural networks. In this paper, the MATLAB neuro fuzzy designer toolbox is used. The designer is capable of applying fuzzy inference techniques to data modeling. The shape of the membership functions depends on parameters. Because of the linear dependence of each rule on the input variables, the Sugeno method (which is used here) is ideal for acting as an interpolating supervisor of multiple linear controllers that are to be applied, respectively, to different operating conditions of a dynamic nonlinear system.

Considering a Sugeno type of fuzzy system having the rule base.

1. If x is A_1 and y is B_1, then $f_1 = c_{11}x+c_{12}y+c_{10}$
2. If x is A_2 and y is B_2, then $f_2 = c_{21}x+c_{22}y+c_{20}$

and so on the rules.

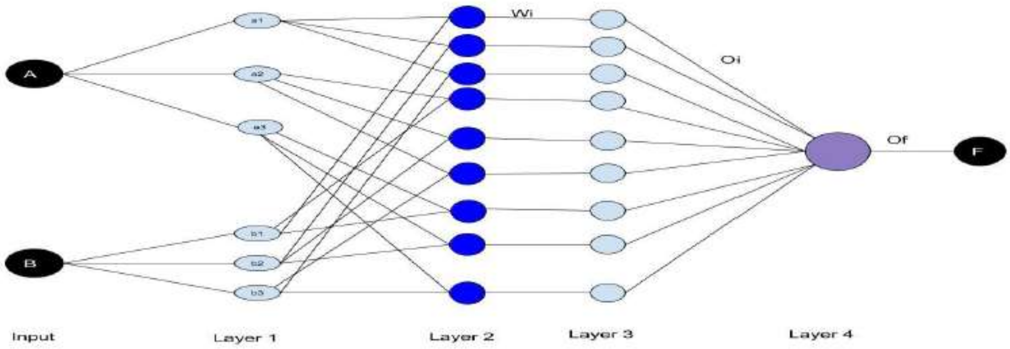

Figure 4. ***ANFIS Structure***

Layer 1:

Each input generates the membership grades of the linguistic label. Example of a membership function (triangular function) is:

$$f(x) = \begin{cases} 0, & x \le x_1 \\ \dfrac{x - x_1}{x_2 - x_1}, & x_1 < x \le x_2 \\ \dfrac{x_3 - x}{x_3 - x_2}, & x_2 < x \le x_3 \\ 0, & x \ge x_3 \end{cases}$$

Similarly, the general membership function for trapezoidal function is:

$$f(x) = \begin{cases} 0, & x \le x_1, \quad x_4 \le x \\ \dfrac{x - x_1}{x_2 - x_1}, & x_1 < x \le x_2 \\ 1, & x_2 < x \le x_3 \\ \dfrac{x4 - x}{x4 - x3}, & x_3 < x \le x_4 \end{cases}$$

Here x_1, x_2, x_3 are the parameter set. The shape depends on the membership function and these parameters. In learning phase these parameters are to be adjusted according to training data. These parameters are called premise

parameters.

Layer 2:

This layer fire strength of the rule is calculated using product of all input signals to the particular node. Also, this layer normalizes the firing strength. In normal ANFIS, these two processes are done in two different layers.

$$\omega_i = f_1 \times f_2 \quad \text{and} \quad \varpi_i = \frac{\omega_i}{\sum_{i=1}^{n} \omega}$$

Layer 3:

Nodes in this layer are adaptive perform the consequent of the rules:

$$\upsilon_i = \omega_i \bullet f_i \quad \text{where} \quad fi = c_{i1}x + c_{i2}y + c_0$$

The parameters c_{i1}, c_{i2} and c_0 are to be determined and are called consequent parameters.

Layer 4:

This is layer sums all the incoming signals into one output. Here Oi is the output from the third layer.

$$\upsilon_f = \sum_{i=1}^{n} \upsilon_i$$

If we assume the premise parameters fixed, the ANFIS output can be represented as:

$$F = \sum_{i=1}^{n} (\omega_i \bullet f_i) \Big/ (\sum \omega)$$

The hybrid optimization method is a combination of least-squares and back-propagation gradient descent method. This learning algorithm adjusts both the premise and consequent parameters to match the training data output. Each epoch has two passes, one forward and another backwards. The forward pass adjusts the consequent parameters using least-square method. Error is calculated at this point and the error is sent backwards which help in adjusting the premise parameters. The backwards adjustment is done using gradient descent method. Hybrid method is faster comparing with original back propagation. The dataset we used is a 50% random sample of the patients with “high-risk” diabetic retinopathy as defined by the Diabetic Retinopathy Study (DRS). Each patient had one eye randomized to laser treatment and the other eye received no treatment, and has two observations in the data set. This study has used the eye not treated to determine the risk. The time of visit by patients is every three months. Survival times in this dataset are the actual time to vision loss in months, minus the minimum possible time to event (6.5 months). The parameters taken into consideration are: Laser type - Xenon (0), Argon (1), Eye - Left eye (0), Right eye (1), Age - age at diagnosis and Futime - time to loss of vision or last follow-up.

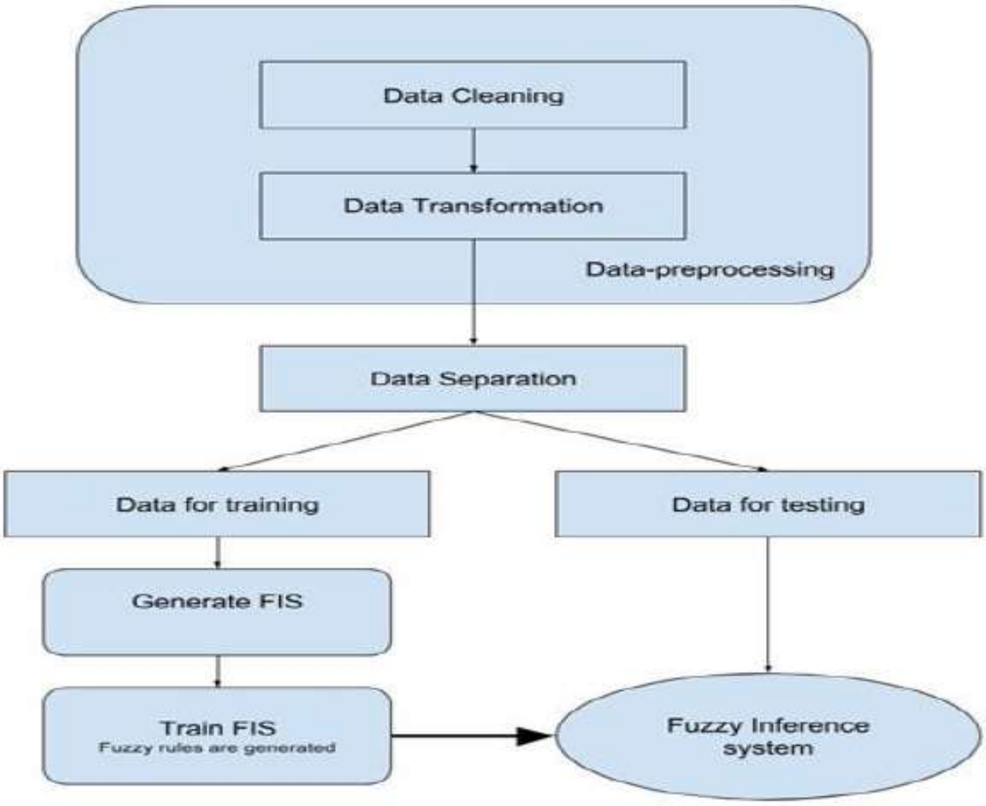

Figure 5. Process Flow Diagram

Data cleaning- Remove unwanted columns like type, id, and risk. Data transformation - The values such as Xenon from type of laser, and right from eye is converted to 1 and 1 respectively for better processing. Data separation- The first 50 entries were taken from the above data for training and the rest was kept for testing. The training data is used to generate and train fuzzy inference system. And the data separated for testing will be used for checking the validity of the system.

While training the FIS (Fuzzy inference system), the grid partitioning technique was used. This technique, generates a single-output Sugeno-type FIS by using grid partitioning on the data. The optimization method used was hybrid method. The number of epochs was kept at 5 and the error tolerance was kept as default. The training process stops whenever the maximum epoch number is reached or the training error goal is achieved. During iterative training of a **neural network**, an **Epoch** is a single pass through the entire training set, followed by testing of the verification set. These inputs use simple trapezoidal functions. For the age variable the membership functions are:

$$\mu Juvenile = \begin{cases} 1, & x \le 10 \\ \frac{20-x}{10}, & 10 < x \le 20 \\ 0, & x > 20 \end{cases} \qquad \mu adult = \begin{cases} 0, & x \le 8,\ 47 < x \\ \frac{x-8}{12}, & 8 < x \le 20 \\ 1, & 20 < x \le 36 \\ \frac{47-x}{11}, & 36 < x \le 47 \end{cases}$$

$$\mu old = \begin{cases} 0, & x \le 36 \\ \dfrac{x-36}{11}, & 36 < x \le 47 \\ 1, & x > 47 \end{cases}$$

And the membership functions for the variable futime are:

$$\mu verylow = \begin{cases} 1, & x \le 10 \\ \dfrac{25-x}{15}, & 10 < x \le 25 \\ 0, & x > 25 \end{cases}$$

$$\mu enough = \begin{cases} 0, & x \le 10 \\ \dfrac{x-10}{15}, & 10 < x \le 25 \\ 1, & 25 < x \le 47 \\ \dfrac{60-x}{13} & 47 < x \le 60 \\ 0, & 60 < x \end{cases}$$

$$\mu healthy = \begin{cases} 0, & x \le 47 \\ \dfrac{x-47}{13}, & 47 < x \le 60 \\ 1, & x > 60 \end{cases}$$

The number of fuzzy rules generated was 36 by the adaptive neuro system.

Modeling ANFIS:

1. Create local workspace variables for test and train data in the MATLAB command window. Open the variables by double clicking the variable name in the workspace.
2. Inset the training data and testing data in the cells of the variables
3. Open the ANFIS editor from application tab or giving a command "anfisedit" in command window.
4. Load the training data first and generate the FIS by selecting grid partitioning on data.
5. The FIS model structure will be generated and can be viewed in structure (Figure 3 was generated using this step).
6. Now the structure needs to be trained. For our problem we used hybrid optimization and we set epochs to 5.
7. Clicking on train now button trains the FIS. Training involves adjusting the membership function parameters.
8. Insert the testing data in variable using aforementioned method and test the system (Figure 5 was obtained after this step).

The following figure shows the neural model structure generated by MATLAB ANFIS editor.

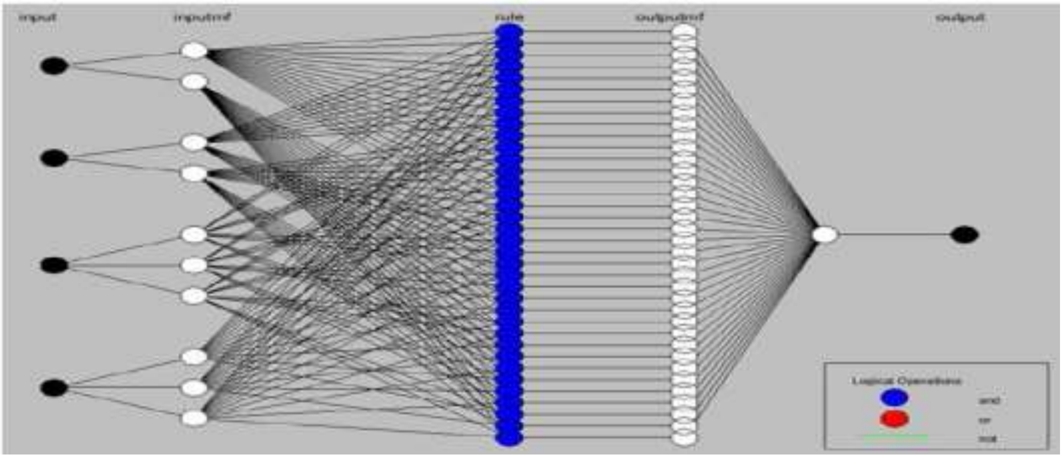

Figure 6. Neural Model Structure of the System

The first four black dots represent the inputs which are age, laser, fulltime and eye. In the next layer the white dots represent the input membership functions respectively to the inputs. The blue dots represent the rules for the membership functions which are created by the ANFIS system by itself. The connections from white dots to the blue dots represent the inclusion of membership function in the rule. The rules produce a part of the output which is combined to form one output.

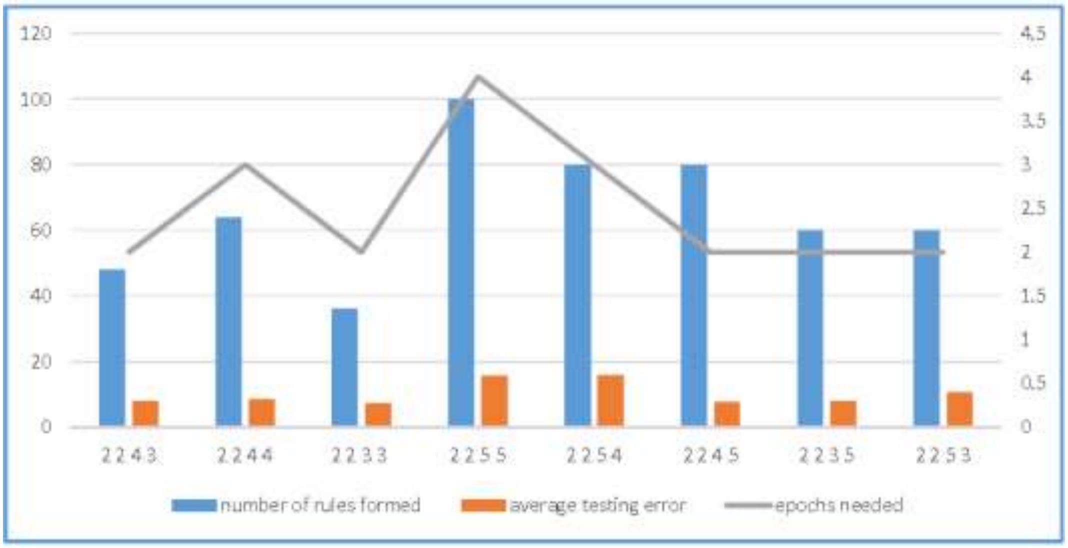

Figure 7. Comparison of Average Error Rates, Number of Rules Formed and Epochs Needed for Different Number of Membership Functions

The above graph shows the comparison of number of rules formed, average testing error and epochs needed. As we can see that the average error rate is lowest in formation with 2, 2, 3 and 3 membership functions. Also, the number of rules formed is less in the formation leading to faster. The number of rules formed is 36. The average error for this formation is 7.1% which is the lowest compared to other formations. The next best formation in terms of average error rate is 2, 2, 5 and 3 at 7.9% and very close to this the formation 2,2 4 3. The number of epochs are equal to the first formation but the number of rules increase. The other formations follow with increased number of rules or epochs in terms of the average error rate.

4. Implementation and Results

The following figure displays the actual values (blue dots) and predicted values (red crosses). The y axis represents the risk value while the x-axis represents the test cases in the testing dataset. As seen in the figure most of the red crosses are in the center cluster where the blue dots dominate.

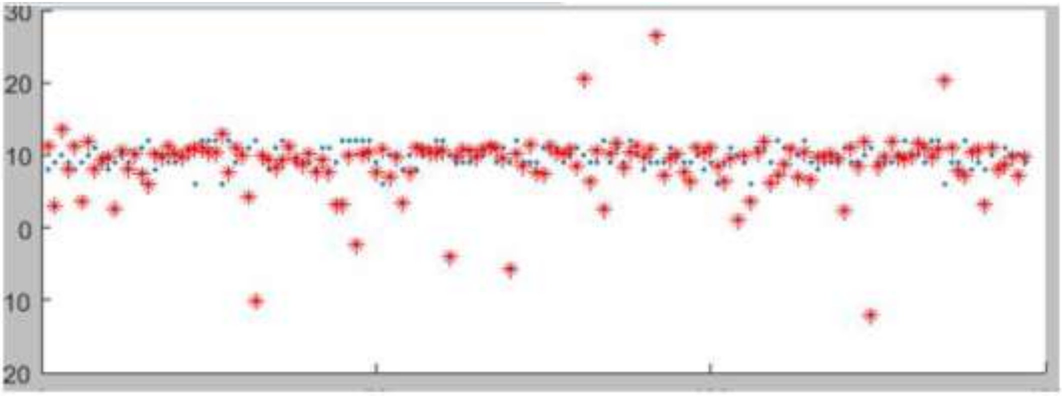

Figure 8. Results of Testing Data (red crosses) Compared to Real Results (Blue dots)

The following table contains the risk values from rule viewer of MATLAB from the generated FIS of some selected inputs.

Table 1. Risk Values for Selected Input Values

Serial Number	Type of Laser	Eye	Age	Futime	Output(Level of risk)	Risk Level
1	Xenon	Left	28	32.8	14.3	High
2	Xenon	Left	28	15.4	14.8	High
3	Xenon	Left	31.5	2.6	14.2	High
4	Xenon	Right	28	15.4	19	High
5	Xenon	Right	28	40.2	16.5	High
6	Argon	Right	28	40.2	6.5	No
7	Argon	Right	39.2	40.2	15.4	High
8	Argon	Right	44.1	17.3	13	High
9	Argon	Left	44.1	17.3	9.9	No
10	Argon	Left	22	17.3	9.2	No

Confusion Matrix:

True negative are the cases when the prediction by the system was no and the actual result was also no. Here the number of true negatives (TN) = 25

False negative are the cases when the prediction by the system was no but the actual result was yes. Here the number of false negatives (FN) = 4

False positive are the cases when the prediction by the system was yes but the actual result was no. Here the number of false positives(FP) = 10

True positive are the cases when the prediction by the system was yes and the actual result was also yes. Here the number of true positives (TP) = 159

1. **Accuracy** refers to the proximity of measurement results to the actual value = (TP+TN)/total = (159+25)/198 = 0.929
2. **Misclassification rate** is the measure of wrong calculation by the system = (FP+FN)/total = (10+4)/198 = 0.070
3. **True positive rate (Sensitivity)**measures the proportion of positives that are correctly identified = TP/actual yes = (159)/ 163 = 0.97
4. **False positive rate** is how often does the system predict true when actually the result was false = FP/actual no = (10)/ 35 = 0.285
5. **Specificity** measures the proportion of negatives that are correctly identified = TN/actual no = 25/35 = 0.714
6. **Precision** refers to reproducibility of the measurement = TP/predicted yes = 159/169 = 0.940

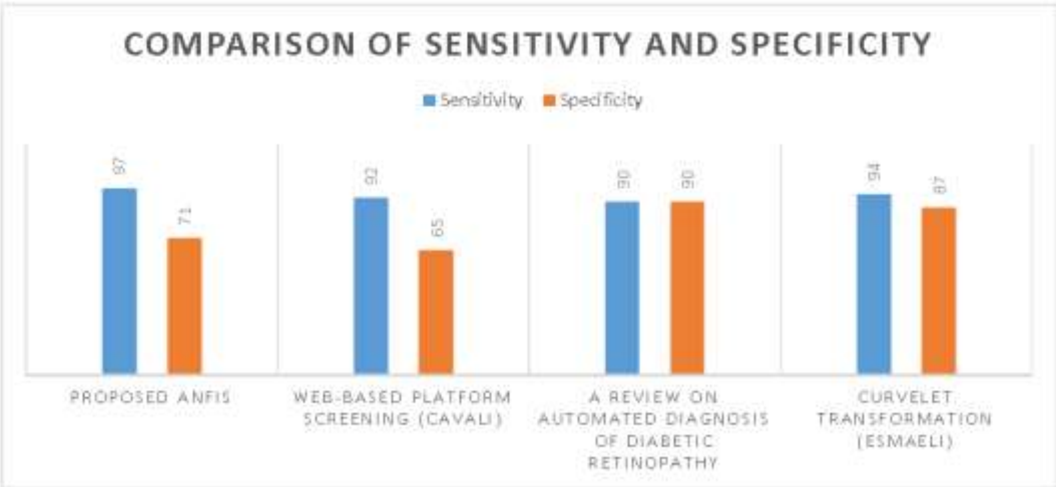

Figure 9. Comparison Graph for Performance Parameters

The ANFIS method proposed in the paper has produced very accurate results. Dataset were divided in 60% for training and 40% for testing, and the error was found to be minimal. The attributes focused on the eye condition and treatment method. The accuracy was found to be 93% and the precision was found to be found 94%. The specificity was about 71% and sensitivity of the model was 97%. Compared to web based platform by Cavalli in 2015, the sensitivity is more by 5% and specificity is increased by 6%. The method can be considered to be dependable, fast and robust means of diagnosing diabetic retinopathy.

6. Conclusion

In Moreover, the use of this system will help patients, doctors and many health practitioners in saving time and cost compared to conventional methods. The treatments are only necessary if the screening attains a score of 13 and above using this system. The methods include laser treatment, injections of medications, or operation to remove scar tissue. Avastin (bevacizumab), Lucentis (ranibizumab), and Eylea (aflibercept) are anti VEFG drugs used by US for the treatment of diabetic retinopathy. Focal/grid macular laser surgeries are used for curing the disease if anti VEFG drugs do not show any improvement in curing the disease. To reduce the swelling Laser are used. Blood vessels which highly damage the retina are reduced using panretinal photocoagulation surgery.

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