An Alzheimer's Disease Prediction System using Fuzzy Logic

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ABSTRACT: *Information Technology has modernized the approaches of the investigation done by the medical researchers as well as the experts in the clinical practice. Recent medical tools allow recording of massive volumes of patient data, which paves the way to know about the disease thoroughly and it helps for better healthcare measurements. But the medical experts in the clinical practice are unable to get benefit from the massive volumes of patient data. Thus there is a need for the computer based techniques, which supports the medical experts while making the diagnostic decisions. Thus the decision support system provides an intelligent report about the patient status based on the symptoms, lab reports and patient related information. Such Decision Support system helps to enhance the patient healthcare measures automatic based on knowledge discovery. Thus, this paper developed a software tool to validate the clinical data by implementing Fuzzy Logic method and data visualization methods for estimating the stages of the patient affected by the Alzheimer's disease. Here SAGE Test and ELISA test reports were used as biomarkers to analyze the stages of the Alzheimer's disease.*

1. Introduction

In the medical domain, a massive extent of knowledge is needed, for even to resolve apparently simple health issues. Nowadays medical experts were in need to recollect and apply information of a colossal array of documented related to various health issues based on disease presentations, diagnostic parameters, combination of drug therapies and guidelines. Though the Medical expert's perceptive capabilities are restricted because of the factors like multitasking, limited reasoning and memory capability. Consequently, it's not possible for an unaided medical expert to create the correct decision on every occasion.

Unluckily, the increasing rate of knowledge generated by medical developments makes worse the physician's task. The decision making process incorporates the technique of data discovery. Many researchers think about data processing techniques as an approach to make an intellectual decision making tools. The potential of Computer Technology based tools to deal with the medical decision making problems are recognized half a century past and several other algorithms are developed to construct an automatic Decision Support Systems for a range of medical fields.

Decision support systems (DSSs) are some software tools which help the users to make decisions based on analytical and scientific methods. Such methodology was built based on the algorithms and techniques from the fields of Logical modelling, Optimization and stochastic modelling, decision analysis and simulation. Usually Decision Support System will analyse, interpret, execute and visualize the objects involved in the scenario.

Now-a-days, the increasing popularity in data warehousing, online analytical processing and SPM i.e, Supply Chain Management paves the way in the development of Decision Support System.

Such Decision support tools could support to make decisions in problems containing the sharing of infrequent resources, risk management, and it is needed to balance the incompatible objectives. Building a good Decision Support System needs a well expertise in Problem analysis, programming and user friendly environment. By implementing the Decision support system in a well and wise manner will improve the system in a commendable manner.

The process involved in the further sections of this paper was mentioned as below. Literature Review is presented in section (II), a detailed explanation about the Alzheimer's disease is presented in section (III), the Methodology implemented in the decision support system is mentioned in section (IV), the implementation part of the methodology is discussed in section (V) and the final conclusion is presented in section (VI).

2. Literature Review

Automatic system oriented investigation of patient data can calculate the information with good analytical precision, while comparing with the experienced Medical practitioner [1]. Such automatic tool may help to manage and control the increasing vast amount of patient's data records and such tool can improve the quantity of information that a medical practitioner can examine, and which mines the interesting patterns from the vast of the clinical data [2].

Clinical decision support systems (CDSS) have exposed their prospective in reducing medical errors and growing health care quality and proficiency [3]. Visualization techniques for investigating biomedical and historical data are already usual in the research field [4], and innovative clinical information visualization tools are frequently being established [5].

Alzheimer Disease is the utmost reason for dementia, Among the 34 millions of dementia cases around the world wide, 2/3 patients were affected by Alzheimer Disease [6]. Dementia is a common word that denotes to a collection of symptoms signifying problems with memory or understanding. The word dementia does not expose the unique reason for the problems mentioned above and dementia is not a disease: it is the clinical indicator of a disease. There are countless probable causes of dementia, more or less of which are reversible [7].

While the cause and effect of Alzheimer Disease are not so far fully understood, the physiological process of Alzheimer Disease can be identified in the preclinical phase from several intelligent studies [8]. Alzheimer Disease is a neurodegenerative disease that is one of the important foundations of dementia due to irreversible death of brain cells, which also increase speed of cell death as the disease progresses [9].

During the course of the pathological process, restrained cognitive variations and impairment occur, and finally the memory and cognition of the person weaken towards clinical dementia [10].

Alzheimer Disease is the reduced concentration of amyloid protein in the Cerebro Spinal Fluid (CSF). This reduction in CSF is followed by an incrementation of amyloid in the brain, which can be noticeable using positron emission tomography (PET) amyloid imaging technique. Next, the increase of tau proteins in the CSF and the brain tissues transforms the brain metabolism, causing functional and structural neurodegeneration. These are detectable using fluorodeoxyglucose (FDG) PET and essential magnetic resonance imaging (MRI), respectively.

The current suggested treatments, nonpharmacological interventions and medications for treating Alzheimer Disease are most in effect at the earliest stages of the disease, highlighting the significance of early diagnosis of Alzheimer Disease at the MCI phase is mentioned in [11].

At present, there is no medicine that would reverse or stop Alzheimer Disease advancement altogether, but when one is found, it is expected to afford greatest benefit if started early. However they are important for clinical diagnostics, the sensitivity and specificity of all current biomarkers of Alzheimer Disease are somewhat poor when considered in isolation.

One more recent development made probable by novel biomarker acquisition technologies is a hypothetical model of Alzheimer Disease evolution by Jack et al. [12], showing the chronological dynamics of different biomarkers in relative to the Alzheimer disease stages. This hypothetical model provides a chronological aspect to biomarkers that should also be measured in the diagnostic process. Such evaluation system is defined not only as a CDSS but also as a research tool that could help clinicians to decide the most relevant parameters for diagnosis of Alzheimer Disease and its cause [13]. An expert system for discovery new knowledge and up-and-coming rules to support the analytical process of dementia was recently introduced in [14].

3. Alzheimer's Disease

Alzheimer's disease is a deteriorating brain disease that causes difficulties with Memory, Thinking and Behaviour. Such things are not a usual sign of aging. Day by day the Alzheimer's Disease gets worse.

Though symptoms will vary wide, the primary problem for many of the people is forgetfulness, which affect severely on their ability to perform the simple task at home or at work or to get pleasure from hobbies. The Alzheimer's disease may lead someone to become confused, stray in familiar places, misplace things or have suffering with language. It may be straight forward to clarify away uncommon behaviour as a part of normal aging particularly for somebody who looks physically healthy.
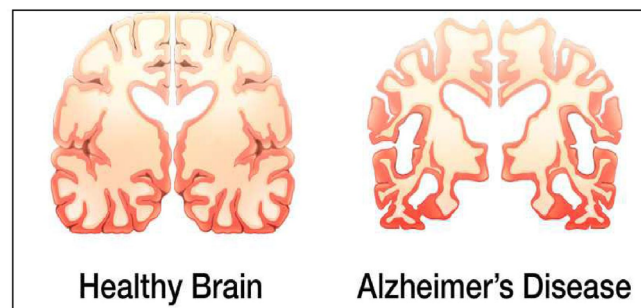

Figure 1. Comparison of Normal Brain & Alzheimer's Disease Brain

It's the foremost common reason behind dementia. Dementia is characterised as decay in memory, language, problem-solving and alternative psychological feature skills that affect a person's ability to perform everyday activities. This decay happens as a result of nerve cells i.e., neurons, which is a components of the brain involved in Cognitive function are broken or destroyed. In Alzheimer's disease, the destruction and damage of neurons eventually have an effect on alternative components of the brain, as well as those who enables someone to hold out basic bodily functions like walking and swallowing. People, who were suffering in the final stages of the Alzheimer's disease are bed-bound and need cautious and continuous care. Alzheimer's disease is finally fatal.

3.1 The Key Role of Plaques and Tangles in Severing the Alzheimer's Disease
The brains of the individuals affected with Alzheimer's Disease have abundant of plaques and tangles. The deposit of a protein fragment known as beta-amyloid is called Plaques, which forms up within the areas between nerve cells. Tangles are located and forms up inside cells, it is a twisted fibers of an additional protein known as 'tau'. Though post-mortem studies show that almost all individuals will have some plaques and tangles which will grow as the age increases day by day. According to [16], If the growth of plaque and tangles were combined along with Alzheimer's Disease will develop those plaque and tangles in high extreme, which will spread to other regions of Brain also. Such patterns should be predict in the beginning itself before spreading. Even after a thorough study, Medical experts and scientist can't exactly know what role plaques and tangles play in

severing Alzheimer's disease. Most of the medical experts consider that these plaque and tangles will disable or block communication amongst nerve cells and mess up the cells processes, which have to be compelled to survive. The damage and death of nerve cells grounds memory failure, personality changes, issues in completing daily activities.

Figure 2. Plaque and Tangles spreading from one area to other areas

3.2 Symptoms of Alzheimer's Disease
Some early and later symptoms were listed from [15] to identify the stages of the Alzheimer's disease which will help in the right way at medication.

• **Early Symptoms**

• Finding harder to remember certain things.

• Sometimes asking the same question again and again.

• Having trouble in calculating money as well as paying bills

• Sometimes getting lost.

• Putting some items in odd places or even losing them.

• **Later Symptoms**

• Forgetting the regular activities like brushing teeth and combing hair.

• Often confused about the people, place and time.

• Even forgetting the names of the very common items like desk, apple or house.

• Frequently wandering away from home.

3.3 Alzheimer's Disease Affecting the Process of Brain
The fluctuations that happen within the brain are the very beginning stage of Alzheimer's disease, i.e it is at the microscopic level, but it can be identified after the observation of primary signs of memory loss. The brain has hundred billion nerve cells called as neurons. Every neuron connects to several other neurons to make a communication network with brain. In addition to the neurons, the brain includes cells specialised to upkeep and promote other cells.

Each Collection of nerve cells has special jobs. Some neurons are concerned with thinking, learning and memory. Others neurons help us to see, to hear, to smell and to tell the muscles that when to move. Brain cells will operate like a small industrial unit.

They receive supplies, construct instrumentation, generate energy, and good in eliminating waste. In addition to the above said process, cells will also store information, process and communicate with each other. To keep whole thing running in a right way it needs coordination among the cells as well as huge quantities of energy and oxygen.

The Alzheimer's disease prevents the cell from running, it produces the breakdowns in one area which caused problems in other

areas of brain also. As the destruction spreads to all or major parts of the brain will cause cells to lose their skill to do their jobs alone and finally the patient will die.

4. Research Methodology

The overview of the Research Methodology designed in this paper is depicted in the figure 3. This entire process is divided into four Phase, such as,

• Phase I: Input Interface

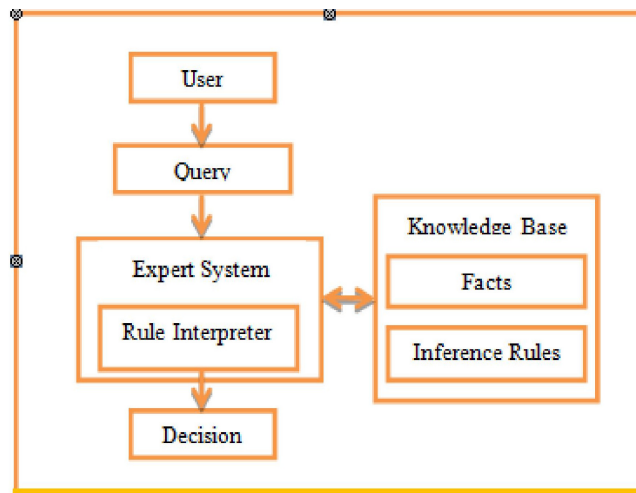• Phase II: Query Formulation (Selection of Attributes)

• Phase III: Expert System

• Phase IV: Decision

Figure 3. Overview of Alzheimer's Disease Prediction System Methodology

4.1 User Interface
User Interface phase creates a user friendly environment to get and hold the information provided by the user as an input for the system. Here by using the figure feature in Matlab a guide environment, which is like a form design, is created to act as a bridge between the user and the system

4.2 Query Formulation
Query Formulation phase contains the queries related to the input domain. The queries given to the system is in two forms. One is in the form of Patient Questionnaire, which contains 10 sample questions and another is in the form of ELISA Lab test Report [19]. A Famous test name SAGE Test (Self-Administered Gerocognitive Examination), which is discover early signs of cognitive, memory or thinking impairments. SAGE test calculates the thinking abilities of the patient and helps doctors to identify how well the brain is working. According to [18] Medical Researcher proved that 80% of the problems along with the memory like, mild cognitive Impairment (MCI), Alzheimer's disease and early dementia will be identified by this SAGE Test. SAGE Test contains 10 Questions. Each question in SAGE Test includes Memory Test, Problem Solving Test, Drawing Test, Judgement Test, Vision Test, Mood Test, Recalling Test, Understanding and Working Test, Finally Word Search Test. The Average time needed to complete the test is 10 to 15 minutes. A printed Question Paper will be given to the patient and marks will be given according to the answers. Marks for each question ranges from $0 - 1$. Correct answer score rages from 0 onwards to wrong answer ranges to 1. Finally the answers for all the 10 questions will be added and now the result for the SAGE Test is stored.

And on the other hand the ELISA Lab test (enzyme-linked immunosorbent assay) contains five tests which were obtained from the cerebrospinal fluid from the spinal cord. Here also the data ranges from 0-1 for each test. No pathology ranges from 0 onwards to pathology ranges to 1. Finally the results were added and now the result for the ELISA Test is stored.

4.3 Expert System

Expert System phase implements the Fuzzy Logic Rule interpreter to generate the rules based on the rules in the knowledge base. Based on the results of the SAGE Test and ELISA Test Fuzzy Rule generator generates the rules based on the number of Fuzzy input and output variables. Here two input variable namely, SAGE Test and ELISA Test, and one output variable namely, Alzheimer's Report were used. The Fuzzy sets for the Input variables and output variable were listed below:

• SAGE Test

{Normal, Mild, Moderate, Severe}

• ELISA Test

{No, Yes}

• ALZHEIMER Report

{Normal, Pre-Clinical AD, MCI Due to AD, AD with Dementia}

Field	Name of the Field	Range	Fuzzy Sets
Input	SAGE Test	0 -2 3-5 6-7 8-10	Normal Mild Moderate Severe
Input	ELISA Test	0-2 3-5	No Yes
Output	ALZHEIMER Report	0-3 4-5 6-7 8-9	Normal Pre-Clinical AD MCI Due to AD AD with Dementia

Table 1. Representation of Fuzzy Variables & Fuzzy Sets

In the Fuzzification phase the SAGE result and the ELISA Result were in numbers and these numbers were converted in the fuzzy Crisp sets listed above, based on the Input field ranges.

The Gaussian Member function is defined by a central value **m** and a standard deviation **k > 0**. The smaller k is, the narrower the "bell". The Gaussian member is were used to create member functions for the Input and output fuzzy Crisp Sets based on the Ranges mentioned here.

For the SAGE Test, 4 Gaussian Member functions were generated in the range of 0 to 2 for Normal, 3-5 for Mild, 6 to 7 for Moderate, and 8 to 10 for Severe.

For ELISA Test 2 Gaussian member functions were generated in the range of 0 to 2 for No Pathology and 3 to 5 for Pathology.

For Alzheimer's Report 4 Gaussian member functions were generated in the range of 0 to 3 for Normal, 4 to 5 for Pre-Clinical AD, 6 to 7 for MCI Due to AD, 8 to 9 for AD with Dementia.

$$\mu_{A^i}(x) = exp\left(-\frac{(c_i - x)^2}{2\sigma^2_i}\right) \tag{1}$$

Where c_i and σ_i are the center and width of the ith fuzzy set A^i.

which was explained in the Fuzzification, Inference Engine and Defuzzification Process.
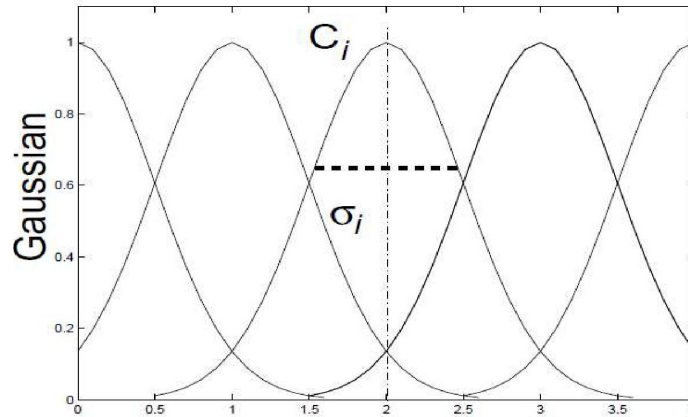
4.4 Knowledge Base

Figure 4. Gaussian Membership calculation for Fuzzy Sets

Knowledge Base contains Facts such as Real things about the system and the inference rules present in it Contains rules provided by the domain experts. This Knowledge base act as a model for the system. The data will be tested based on the model data. Here SAGE test and ELISA Test act as inputs to the rule and Alzheimer's Report act as an output. The input rule given to the SAGE Test is Normal, Mild, Moderate and Severe at the same time the input rule given to the ELISA test is Yes and No. Finally the Alzheimer's report in four stages like, Normal, Pre-Clinical AD, MCI due to AD and AD with Dementia. Instead of fuzzy sets, numbers were used to indicate the rules in the rule generator. First column denotes the SAGE Test, Second column denotes the ELISA Test, and the third column denotes the ALZHEIMER Report.

```
ruleList = [ 1 1 1 1 1
             2 1 2 1 1
             3 2 3 1 1
             4 2 4 1 1];
```

Table 2. Numerical Representation of Rule List in Matlab

1. If (SAGE TEST is Normal) and (ELISA LAB TEST is No) then (ALZHEIMER Report is Normal) (1)

2. If (SAGE TEST is Mild) and (ELISA LAB TEST is Yes) then (ALZHEIMER Report is Pre-Clinical AD) (1)

3. If (SAGE TEST is Moderate) and (ELISA LAB TEST is Yes) then (ALZHEIMER Report is MCI Due to AD) (1)

4. If (SAGE TEST is Severe) and (ELISA LAB TEST is Yes) then (ALZHEIMER Report is AD with Dementia) (1)

Table 3. Rules for Fuzzy Expert system in Matlab

4.5 Decision
Decision module generates the final decision based on the expert systems rule. It displays any one results of the Alzheimer's Report in the user Interface as Normal, Pre-Clinical Alzheimer's Disease, Mild Cognitive Impairment due to Alzheimer's disease and Alzheimer's Disease with Dementia based on data generated in the fuzzy Defuzzification process.

5. Experimental Results

In this paper, the Alzheimer's Disease Prediction system was designed and enforced in Matlab. For the experimental study, 70 samples (60 Alzheimer's and 10 Normal) report format was referenced and collected from the Internet. Alzheimer's disease

Prediction System was developed using the Fuzzy Logic Rule Methods based on the results of the SAGE Test and ELISA Test. Figure 5 depicts the User Friendly Environment for Alzheimer's Disease Prediction System.
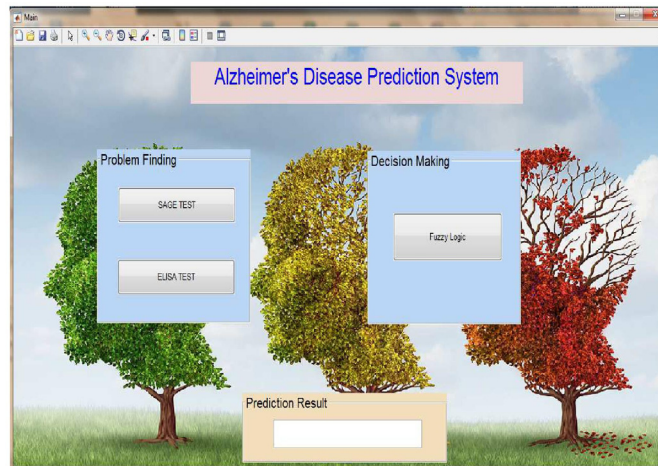

Figure 5. User Friendly environment of Alzheimer's Disease Prediction system

Figure 6 & 7 depicts the 10 Symptoms and Questionnaire for the Alzheimer's disease patient. The first form contains the basic 10 Symptoms of the Alzheimer's disease, if the majority answers were 'Yes' then go for the SAGE Test, else the patient is normal. SAGE Test contains 10 Questions, which analyses the thinking abilities of the patient and the functioning of the Brain. The Form should filled with 'Yes' or 'No' values in the text box, based on the diagnosis of the patient. The Results were filled based on the performance of the SAGE test.
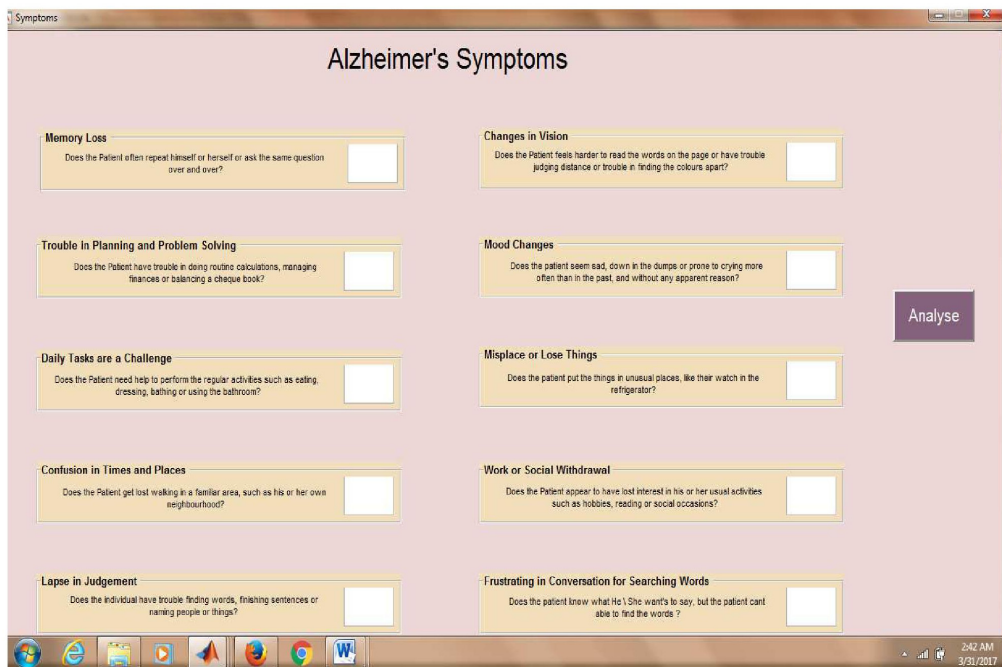

Figure 6. Questions for finding Alzheimer's Symptoms

Figure 8 depicts the ELISA Lab test reports based on the MRI & Amino Fluid Test. The ranges of the inputs are 0 to 1. 0 indicates the lower occurrence of No Pathology and the higher range towards 1 indicates the Presence of Pathology. At the final, the sum of the test reports was taken into accountable for rule generation.

Figure 7. Questionnaire for the patient to analyze and calculate the Alzheimer's Disease
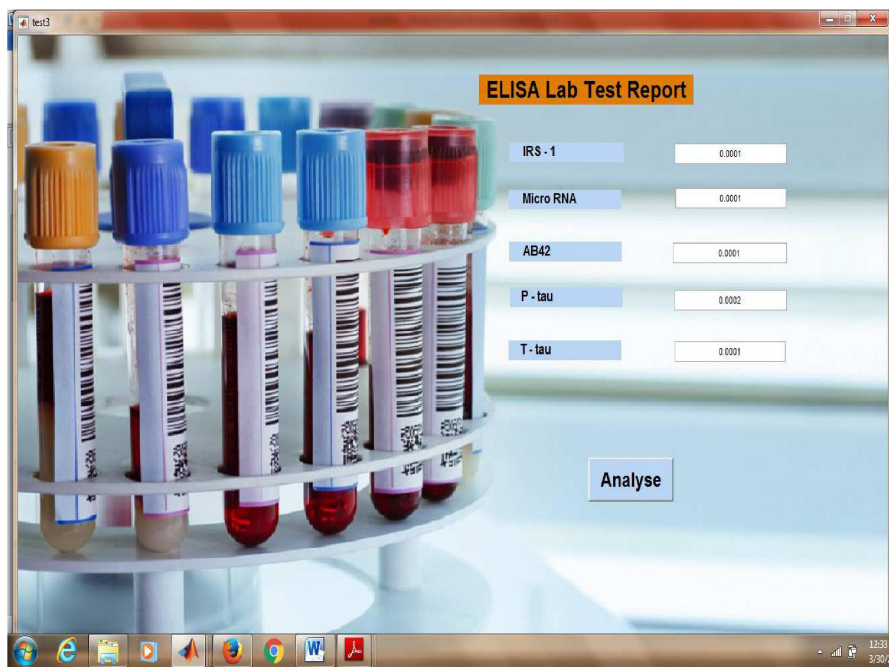

Figure 8. ELISA Lab test Report to predict Alzheimer's disease System

Figure 9 depicts the Fuzzy Logic Designer for Alzheimer's Disease Prediction system. It contains two Input variables and one Output variables. Mamdani method was implemented for Member function creation and rule generation. Mamdani's method is the most common control systems built using fuzzy set theory. Mamdani-type inference, expects the output membership functions to be fuzzy sets for that which finds the centroid of a two-dimensional function.

Figure 10 & 11 depicts the degree of Membership for ELISA Lab test and SAGE test. A Membership Function is a curve that defines how each point in the input space is mapped to a degree of membership value, between 0 and 1. SAGE Test Ranges from

0 to 10. But ELISA Test Ranges from 0 to 5. Here the member function was created using Gaussian Bell.
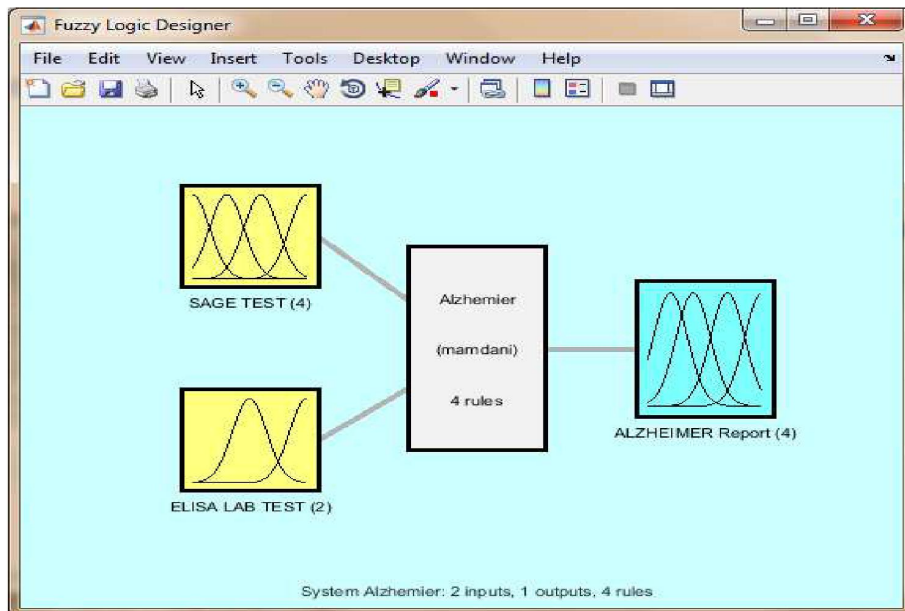

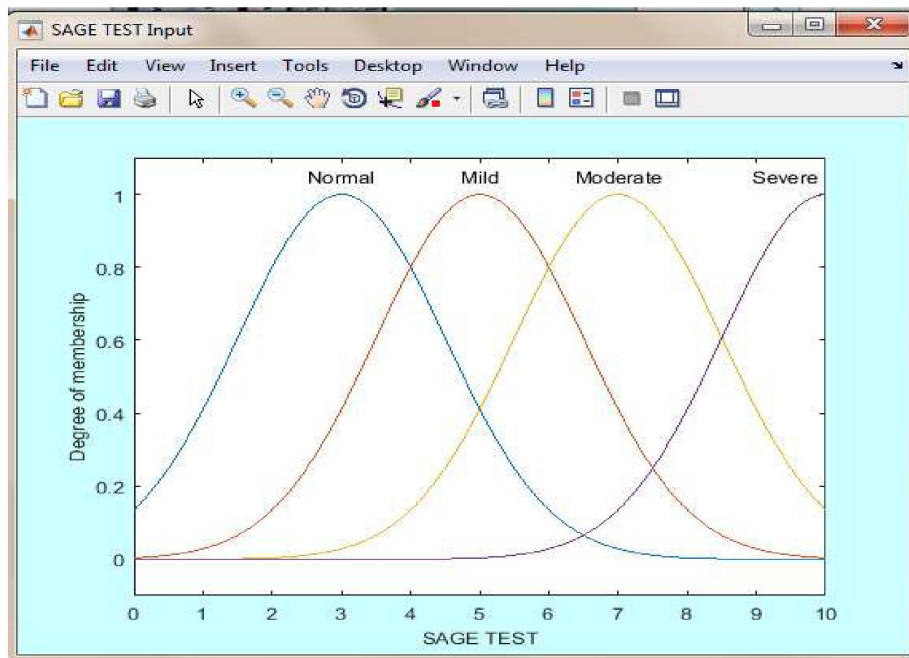Figure 9. Fuzzy Logic Designer for Alzheimer's Disease Prediction system

Figure 10. Gaussian Wave member ship for the SAGE Test

Figure 12 depicts the degree of Membership for the Alzheimer's Report.

Figure 13 depicts the final overall report for the Alzheimer's Disease based on the Results of the SAGE test and ELISA test.

Figure 14 depicts the final output of the Alzheimer's Disease Prediction system based on the knowledge Rule Mining Technique used in the Fuzzy Expert System.
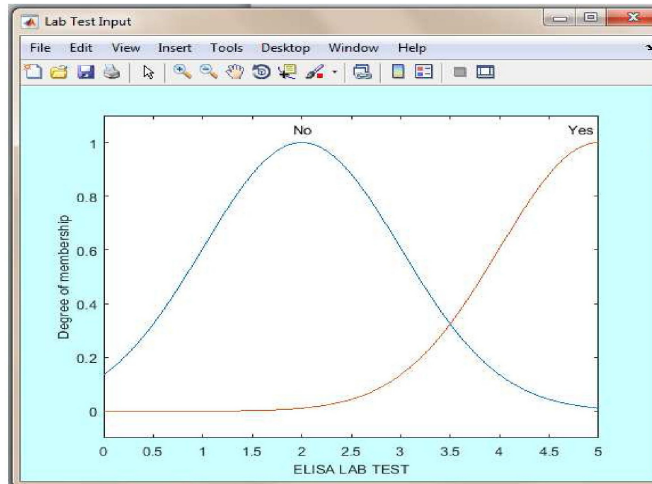
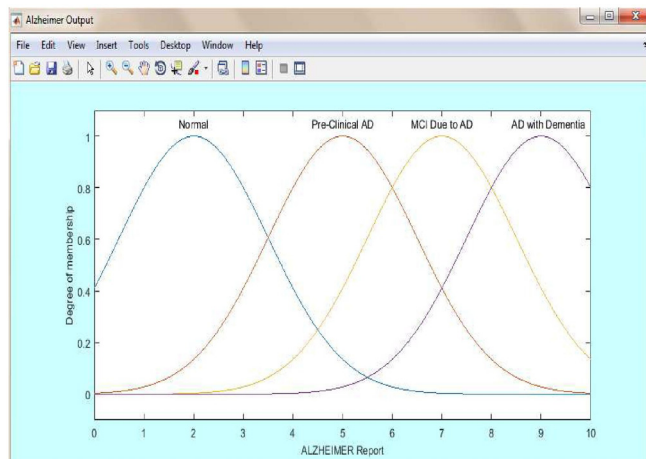Figure 11. Gaussian Wave member ship for the ELISA Lab Test

Figure 12. Gaussian Wave member ship for the Alzheimer's report
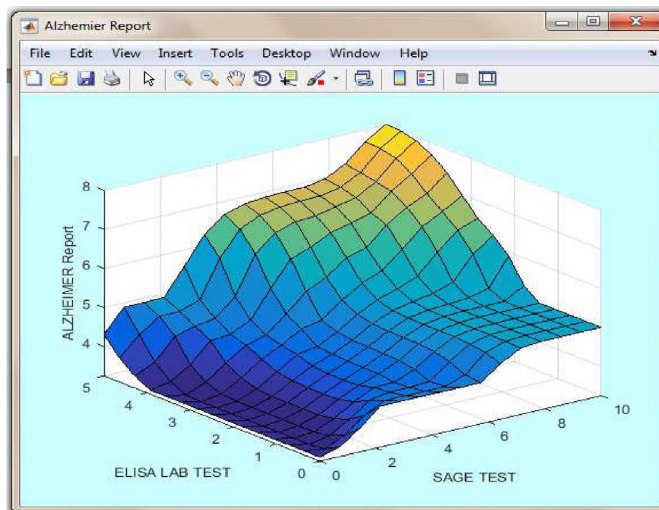

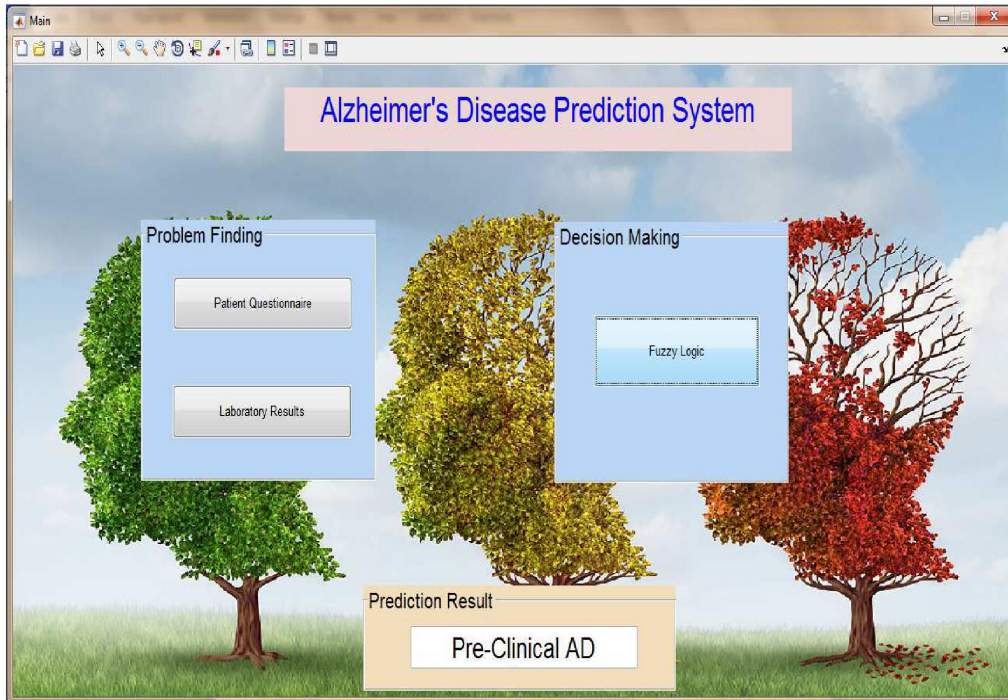Figure 13. Report of Fuzzy Logic for Alzheimer's Disease Prediction

Figure 14. Final Result for Alzheimer's disease Prediction system

Based on the outputs of SAGE Test and ELISA Test, the report for Alzheimer' Disease was generated using the Alzheimer's Report Membership Function, which classifies the result as four stages like, Normal, Pre-Clinical AD, MCI due to AD and AD with Dementia. The final output will be displayed in the text box provided in the bottom of the Main screen.

6. Conclusion

In this paper, a Fuzzy Logic rule based method was implemented and applied to clinical decision support in Alzheimer's Disease. The research work comprised design, development and evaluation of Alzheimer's disease. A methodology for decision support system was proposed and developed using MATLAB and evaluated using some data visualization graphs and Fuzzy Logic Rule analyzer, finally a software tools called ADPS tool (Alzheimer's Disease Prediction System tool) was implemented for predicting Alzheimer's Disease using the SAGE Test report and the ELISA Lab Test. This tool will act as an automatic assistance in diagnosing Alzheimer 's disease even at the early stage. Thus the ADPS Tool allows the medical experts in the clinical practice to evaluate all available patient data and help in identifying the Alzheimer's Disease accurately.

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