# THE USE OF ARTIFICAL NEURAL NETWORKS TO STUDY AND IMPROVE NEURAL SYNAPTIC PROMOTERS AND CONNECTIVITY IN ALZHEIMER'S DISEASE STATES

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*Abstract* – **One of the most complex neuro-degenerative diseases is Alzheimer's Disease (AD), a progressive form of presenile dementia generally affecting aged people. Alzheimer's Disease is an irreversible, progressive disorder in which brain cells (neurons) deteriorate, resulting in the loss of cognitive functions such as judgment and reasoning, memory, and pattern recognition. Scientists estimate that by 2050 around 18 million people will be diagnosed with Alzheimer's Disease. Because of this growing epidemic, finding solutions to this problem is increasingly important. In this project, we establish and investigate new ways of representing synaptic connectivity in normal and Alzheimer's patients, thereby increasing our understanding of neural decision-making and reasoning processes. In achieving this goal, we use known artificial neural network (ANN) architectures, more importantly Auto-Associative Networks. To detect neural synaptic promoters, we train the Auto–Associative Neural Networks on different training datasets and observe its recall and response by measuring its prediction accuracy on test datasets. We evaluated the performance of different artificial neural network architectures to differentiate between network "architectures," which indirectly enable us to know the best "environment" (architecture) for neural synaptic activity. Ultimately, these results have allowed us to find areas where synaptic connectivity is present and where it can be improved. By developing this new capacity to understand and model connectivity in normal and AD states, we hope to eventually strengthen the decreased potential in the disease state through unique repetitive learning and biofeedback techniques – first in our computers and then humans.**

## I. PROBLEM STATEMENT

Alzheimer's Disease (AD) is an irreversible, progressive disorder in which brain cells (neurons) deteriorate, resulting in the loss of cognitive functions, primarily memory, judgment and reasoning, movement coordination, and pattern recognition. In advanced stages of the disease, all memory and mental functioning may be lost. In this context, it is important to include that the central problem of this project is to further understand and eventually improve the neural synaptic connectivity in Alzheimer's patients. By improving neural synaptic connectivity "potentials," we plan to find a probable solution to the Alzheimer's epidemic.

To achieve this, we intend to implement Artificial Neural Networks, more importantly Auto–Associative Neural Networks. Auto–Associative ANNs store single instance items and can be thought of as an accurate depiction of human memory. In an Auto-Associative Network, each pattern presents an input and output and can detect patterns in data sets. Because of such recall and response characteristics of neural networks, they can be used to mimic healthy and unhealthy biological models of the brain. In our work, we plan to perform experiments to improve unhealthy biological networks, by training and testing these networks on pattern recognition, image recognition, and character recognition.

In summation, the detection of the optimal network architecture is extremely important in the eventual cure of Alzheimer's. By detecting these architectures, we can observe areas within the networks where neural synaptic connectivity will be promoted. We can furthermore improve existing connections, which have weak synaptic strengths through repeated re-training of neural networks. Our study has developed 1. a network that mimics normal patient neural connectivity, 2. a deeper understanding of how the connectivity relates to functional processes such as pattern recognition and memory, 3. a new model to computationally represent AD states, and 4. the initial identification and modelling of areas of connectivity susceptible to Alzheimer's problems and determination of how functional improvements could overcome these deficiencies.

## II. ARTIFICIAL NEURAL NETWORKS

In the recent past, there has been extensive interest in artificial neural networks. A neural network is an information processing paradigm, generally composed of a large number of highly interconnected processing elements (neurons) working in "unison" to provide problem solving capabilities. Artificial neural networks have been a technique recently used by scientists in the prediction of data, pattern recognitions, as well as image recognition. Because it's an important tool in pattern recognition and data prediction, we plan to implement this in our project.

An artificial neural network (ANN) is a system inspired by the human brain. Its design is based on a multiple layer network consisting of neurons. These neurons are then connected to neighbouring neurons with varying strengths of connectivity power. Because neural networks are closely related to the structure of the brain, it is utilized in neuroscience and computational neuroscience. The computational neuron, which composes the bulk of artificial neural networks, receives certain inputs and then produces certain outputs. In this context, it is important as the basic unit of artificial neural networks. The artificial neural network is composed of the following design: A string of axons "carrying" certain information weight inputs is connected to a parent neuron, then the parent neuron sums up the information weights of each one of the inputs, and finally the output represents the total sum of the information weights from the inputs. The design of artificial neural networks is composed of a multi – layer network that connect to each other. There is first an input layer that receives an exogenous input from an external source in the "environment" (usually a user) and then an output layer, which is the desired result. Artificial neural networks usually take on the form of a two – tier network, but to improve the strength of a network "architecture" (the shape of the layers), a third layer is computed between the input and output layers. This layer is called the hidden layer and is used to strengthen a network's ability to perform. A hidden layer is extremely important because it provides increased connectivity between the neurons, which makes a network stronger and more capable of reaching a desired result. The more number of hidden layers a network has, the more powerful it is [5].

In general, communications are vital for relaying information from one neuron to another. In an artificial neural network, neurons are connected via a network of paths carrying the output of one neuron as input to another neuron. These paths are normally unidirectional; there might, however, be a two-way connection between neurons if one input goes in the reverse direction. A neuron receives input from many neurons, but produces a single output, which is communicated to other neurons. Connections provide in humans the ability to reason, but in an artificial neural network an ability to reach the desired result. The type of neuron connectivity in artificial neural networks include the following: Fully Connected connection types (each neuron on the first layer is connected to every neuron on the second layer), Partially Connected connection types (a neuron of the first layer does not have to be connected to all neurons on the second layer), Feed Forward connection types (neurons on the first layer send their output to the neurons on the second layer, but they do not receive any input back form the neurons on the second layer) and Bi – Directional connection types (there is another set of connections carrying the output of the neurons of the second layer into the neurons of the first layer). Two other connection types could fall under full or partially connections. These are Hierarchical and Resonance Types described by the following: hierarchical connected connection types are characterized by the neurons of a lower layer which may only communicate with neurons on the next level of layer and resonance connected connection types where layers have bi-directional interactions that continue to send messages across the connections a number of times until a certain condition is achieved [5, 7].

Understanding human learning and memory is an area that is extremely important for the future in developing strategies to fight neuro - degenerative diseases. As humans, we learn from experience; artificial neural networks learn from the adjustment of information weights between the connections. When a network does not perform correctly, we change (adjust is a better word) the information weights assigned to the connections, and consequently the network learns from it (the adjustments). The learning in a particular neural network is dependent upon the type of neural network architecture. The type of learning found in artificial neural networks is various and diverse. Unsupervised learning involves hidden neurons that must find a way to independently organize without help from the outside. In this approach, no sample outputs are provided to the network against which it can measure its predictive performance for a given vector of inputs. This is "learning by doing." Reinforcement learning includes connections among the neurons in the hidden layer that are randomly arranged, then reshuffled as the network is told how close it is to solving the problem. Reinforcement learning is also called supervised learning, because it requires a "teacher." The "teacher" may be a training set of data or an observer who grades the performance of the network. Back – propagation learning involves networks not just given reinforcement for how they are doing on a task. Information about errors is also filtered back through the system and is used to adjust the connections between the layers, improving performance. This is a form of supervised learning.

Ultimately, we used a number of important neural network concepts to fashion our version to model normal patient and diseased brain connectivity. In this study, we use back – propagation learning (supervised learning) because the network filters the errors that occur within the network and adjusts its connections to learn "better." Another technique that is coupled with learning is a learning law. A learning law is a mathematical algorithm that updates connection weights and controls learning by a network. Learning rules are important because they usually describe the relationship between a neuron and the inputs involved. The following are common learning rules vital for artificial neural networks: Hebb's Rule - if a neuron receives an input from another neuron, and if both are highly active (mathematically have the same sign), the weight between the neurons should be strengthened and the Delta Rule - this rule is based on the idea of continuously modifying the strengths of the input connections to reduce the difference (the delta) between the desired output value and the actual output of a neuron. The latter rule changes the connection weights in the way that minimizes the mean squared error of the network. The error is back propagated into previous layers one layer at a time. The process of back-propagating the network errors continues until the first layer is reached. The network type called feed forward / back-propagation derives its name from the above described method of computing the error term. In this project we plan to use back – propagation learning coupled with Hebb and Delta learning rules, providing a tool in determining the optimal network structures. In this project $M_1$ is $E_1$, which represent the learning ($M_1$) and the learning rule ($E_1$). We will again find the optimal network architecture by a combination of $M_1$ is $E_1$. The following were mathematical learning algorithms used:

*Hebb's Rule* - $\Delta w = c\, f\,(\sum w_i x_i)\, x_i$

where - c – learning rate

*i – input*

*$w_i$ – output*

*f – activation function*

*$f(\Sigma w_i x_i)$ – sum of the products of the inputs and output*

*Delta Rule* - $\Delta w = h\, [d_j - f(\sum w_i x_i)]\, f'(\sum w_i x_i)\, x_i$

where - *i – input*

*j – output*

*η – learning rated*

*j – desired value*

$y_i$ *– output*

*[f'(net)] – rate of change of weights with each iteration*

*f – activation function*

$\Sigma w_i x_i$ *– sum of the products of the inputs and outputs*

*Perceptron Rule* - $\Delta w = c\, [d_j - f(\sum w_i x_i)]\, x_i$

where - c – learning rate

*i – input*

*j – output*

$d_j$ *– desired value*

$\Sigma w_i x_i$ *– sum of the products of the inputs and outputs*

Artificial neural networks will provide an important tool in our goal of finding the optimal network structure to model normal patient connectivity. In our pursuit of the optimal network architecture we hypothesize that the particular architecture will promote neural synaptic connectivity the most. The following are diagrams of the mathematical learning algorithms used in this experiment: (Single – Layer Perceptron, Multi – Layer Perceptron, Back – Propagation, Delta, and Hebb Rules)

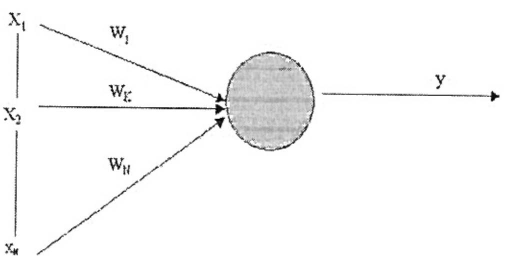

Fig. 1. Single Layer Perceptron

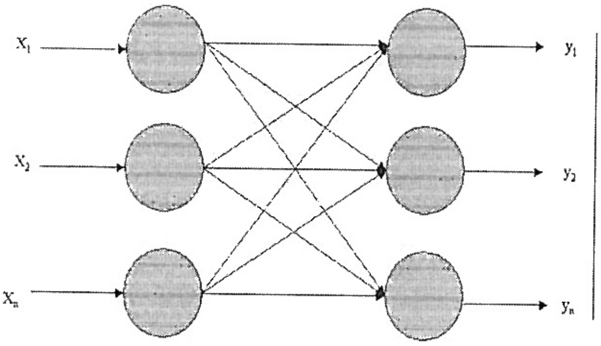

Fig. 2. Multi-Layer Perceptron

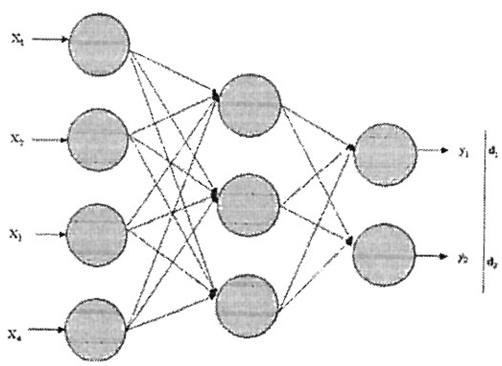

Fig. 3. Bp Network Architecture

## III. AUTO-ASSOCIATIVE NEURAL NETWORKS

Auto – associative neural networks are a type of artificial neural networks detailed in human memory. Auto – associative networks can store single instance items and very accurately represent human memory. This aspect of artificial neural networks is extremely important because it plays a vital role in pattern tasks and recognition. One characteristic of networks and pattern recognition is the iterations (repetitions) that occur. The greater the number of iterations, the better a network is at recognizing patterns. The basic design of the network consists of a two - tier layer network, each layer representing an external environmental source. This makes it easier for a user to input data and receive an output.

Auto – associative networks consist of a two –tier system. There is a layer of "world" units and a "layer" of learning rates. The world units represent the input data from an external environmental source and the learning layer represents the processing of the network to produce an output. We implemented this technique because of its ability for pattern recognition. To test a network for pattern recognition we will first create a healthy biological neuron / normal patient. Then we will create a parity generator. A parity generator is a system that tests a network's prediction accuracy. Datasets of 5 binary numbers (Zeros and Ones) are added to the network. The user, before giving the numbers to the network, randomly predicts the result by his/herself to test the networks ability in predicting the user's result, which is based highly on pattern recognition.

## IV. METHODS

The aim of this project was to detect neural synaptic promoters by identifying and modeling optimal network architecture. To achieve this goal, we performed tests on character recognition, facial recognition, and pattern recognition. We first constructed a healthy biological neuron. We determined whether a network was healthy or not by using a parity generator and prediction accuracy. If the networks prediction accuracy was over ninety percent, we automatically defined it as a healthy system. Anything below ninety percent was an unhealthy system. After determining healthy systems, we performed pattern and character recognition tests on the other varying networks

($M_i$ – $E_i$). After finding the optimal network structure among ($M_i$ – $E_i$), we began to test the optimal network's ability to recognize faces.

The Mi – Ei was used to measure the performance of a network. The Mi – Ei represented the varying models of learning rules and network architecture. In combining the various learning rules, we hoped to determine the best type of network architecture. The following are combinations of the learning models: Delta – Delta, Hebb – Hebb, BP – BP, Perceptron – Perceptron, Perceptron – Delta, Perceptron – Hebb, Perceptron – BP, Delta – Hebb, Delta – BP, Delta – Perceptron, Hebb – Delta, Hebb – BP, Hebb – Perceptron, BP – Hebb, BP – Delta, and BP – Perceptron. In assessing the accuracy of these models, we hypothesized that the optimal architecture would possess highly probabilistic regions of neural synaptic promoters.

Our main plan was to determine whether we could improve unhealthy biological systems by using the optimal network architecture. In performing this, we would gradually degrade the weights until prediction accuracy and accuracy in other testing areas (facial and character) went from 90 percent to 40 percent. By determining the optimal network we wanted to see if it (network) could improve the accuracy of an unhealthy biological system to a healthy biological system.

The following program codes were used to detect the efficiency of the back – propagation and perceptron network models:

The following program codes were used to detect the efficiency of healthy biological networks using back – propagation and perceptron network models:

*A.. Perceptron Matlab Code:*

```
net = newp([0 1; 0 1;0 1; 0 1],1);
        P1 = [0 0 0 0 0 0 0 0 1 1 1 1 1 1 1 1;0 0 0 0 1 1 1
        1 0 0 0 0 1 1 1 1;0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1;0 1
        0 1 0 1 0 1 0 1 0 1 0 1 0 1];
T1 =[1 0 0 1 0 1 1 0 0 1 1 0 1 0 0 1];
net = init(net);
Y = sim(net,P1);
net.trainParam.epochs = 1000;
net = train(net,P1,T1);
P2= [0 0 1 1 1;0 1 0 0 1;0 0 1 1 1;1 0 0 1 1];
Y = sim(net,P2)
x=[0,0,1,0,1];
```

*B. Back – Propagation Matlab Code:*

```
net = newff([0 1; 0 1;0 1; 0 1],[4,4,4,1]);
        P1 = [0 0 0 0 0 0 0 0 1 1 1 1 1 1 1 1;0 0 0 0 1 1 1
        1 0 0 0 0 1 1 1 1;0 0 1 1 0 0 1 1 0 0 1 1 0 0 1 1;0 1
        0 1 0 1 0 1 0 1 0 1 0 1 0 1];
T1 =[1 0 0 1 0 1 1 0 0 1 1 0 1 0 0 1];
net = init(net);
Y = sim(net,P1);
net.trainParam.epochs = 1000;
net = train(net,P1,T1);
P2= [0 0 1 1 1;0 1 0 0 1;0 0 1 1 1;1 0 0 1 1];
Y = sim(net,P2)
x=[0,0,1,0,1];
```

Preliminary results have involved measuring the performance of healthy artificial neural networks (using back-propagation and perceptron models) as well as artificial neural networks mimicking a healthy biological neural system.

## V. MEASURING THE PERFORMANCE OF A HEALTHY NETWORK

We measure the performance of our neuron model $M_i$ by its prediction accuracy or by a normalized sum of the squared errors over the test data. Other parameters for measuring the performance are the number of iterations versus the prediction error.

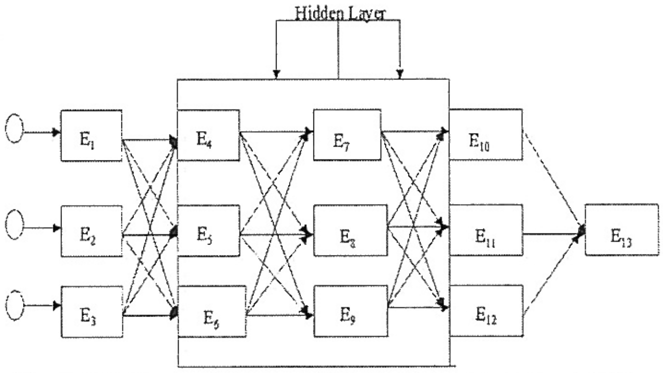


Fig. 4. This Diagram Represents A Healthy Network Including A Hidden Network (E4 And E7)

## VI. ANN MIMICKING A HEALTHY BIOLOGICAL NEURAL SYSTEM

We modeled a healthy biological neural network as a 2-tier fully connected network of basic $E_i$ as the basic learning unit. $E_i$ is a 5-layer ANN with 1 input layer, 1 output layer, and 3 hidden layers. $E_i$ is a multi-layer neural network that uses the delta rule for learning. Model $M_i$ is a 5-layer neural network with one input layer, 3 hidden layers, and an output layer. Each node of the model $M_I$ is $E_I$.

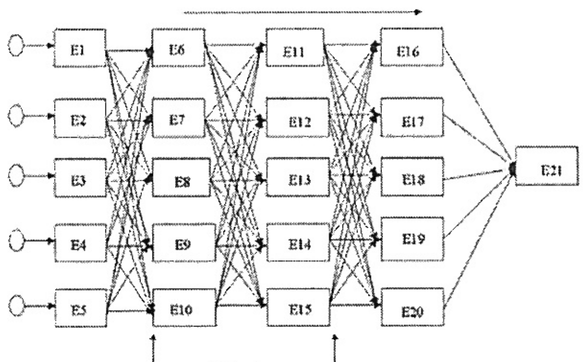


Fig. 5. This Figure Depicts The $E_i$ - $M_i$ Network Model We Developed In This Project

## VII. TESTING THE ABILITY OF ANN TO RECOGNIZE HUMAN FACES

We will first create a healthy ANN network model, which is expected to have reasonably good prediction accuracy in identifying facial image data on which this network has been trained. To mimic early onset of an Alzheimer's affected biological neural system, we intend to corrupt some synaptic connections by altering the stabilized weights in a healthy neural network. Such an action may decrease the subsequent performance of the artificial neural networks. An artificial neural model for the second-stage behavior of an Alzheimer's affected patient may be obtained by further damaging the healthy network by randomly removing healthy synaptic weights. Such a malicious action may further degrade the recall of the artificial neural network. The corrective action includes improving the performance of the unhealthy neural network by randomly eliminating bad connections and appending good connections to yield a better performance with minimal retraining.

## VIII. RESULTS

We trained two neural networks (1) perceptron network, and (2) back-propagation network on the data generated by a 4-bit parity generator. Table 1 below gives the data generated by a 4-bit parity generator.

Table I
Data generated by a four-bit parity generator

| Bit 4 | Bit 3 | Bit 2 | Bit 1 | Output |
|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 1 |
| 0 | 0 | 0 | 1 | 0 |
| 0 | 0 | 1 | 0 | 0 |
| 0 | 0 | 1 | 1 | 1 |
| 0 | 1 | 0 | 0 | 0 |
| 0 | 1 | 0 | 1 | 1 |
| 0 | 1 | 1 | 0 | 1 |
| 0 | 1 | 1 | 1 | 0 |
| 1 | 0 | 0 | 0 | 0 |
| 1 | 0 | 0 | 1 | 1 |
| 1 | 0 | 1 | 0 | 1 |
| 1 | 0 | 1 | 1 | 0 |
| 1 | 1 | 0 | 0 | 1 |
| 1 | 1 | 0 | 1 | 0 |
| 1 | 1 | 1 | 0 | 0 |
| 1 | 1 | 1 | 1 | 1 |

Table II
Results of the neural networks on test data

| Bit 4 | Bit 3 | Bit 2 | Bit 1 | Expected Output | Perceptron Output | BP Output |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| 0 | 1 | 0 | 0 | 1 | 1 | 1 |
| 1 | 0 | 1 | 0 | 1 | 1 | 1 |
| 1 | 0 | 1 | 1 | 0 | 1 | 0 |
| 1 | 1 | 1 | 1 | 1 | 1 | 1 |

The prediction accuracy of a back - propagation neural network is 100%. The prediction accuracy of perceptron neural network is 80%. We were also able to produce graphs that depicted the number of iterations needed for each learning algorithm. The greater the number of iterations needed, the better prediction accuracy the model produced.

## IX. UNHEALTHY BACK-PROPAGATION TYPE NEURAL NETWORK

This report presents the results of deteriorating a healthy back-propagation type neural network model by altering its post-convergence synaptic strengths (weights). The healthy back-propagation type neural model is deteriorated to mimic the weakened synaptic neural connections in the brain of an Alzheimer's patient. The fully connected architecture of our healthy back-propagation type neural network consists of five neurons in the input layer, twelve neurons in the hidden layer, and one neuron in the output layer (resulting in 66 synaptic weights). The healthy network was trained on 5-bit parity generator dataset to produce 100% accurate prediction. The healthy network was iterated 10,001 times to reach its convergence. In Table I, we present the results of one healthy back-propagation type neural network and five unhealthy neural networks (in terms of its prediction accuracy) obtained by deteriorating the healthy neural network. To obtain an unhealthy network, some weights of the healthy model were altered to random values and the new network thus obtained was trained for 10,001 iterations. From Table II, we may observe that as the number of altered synaptic weights increase, the prediction accuracy decreases. Our neural network has been trained with three different sets of initial weights $w_1$, $w_2$, $w_3$, with two different learning rates 0.1 and 0.5. Results in Table III show that the back-propagation network performs well if trained on 100% of the dataset. However, the prediction accuracy degrades as the percentage of training data is reduced to half the original dataset. It can also be observed that as the learning rate decreases, the number of iterations (epochs) increases.

Table III
The Performance Of Healthy And Unhealthy Back-Propagation Type Neural Networks On 5-Bit Parity Generator Dataset

| Network Type | Number of Synaptic Weights Altered | Percentage of Correct Prediction |
|---|---|---|
| Healthy BP network | 0 | 100 |
| Unhealthy BP-1 | 15 | 100 |
| Unhealthy BP-2 | 40 | 84.375 |
| Unhealthy BP-3 | 41 | 81.25 |
| Unhealthy BP-4 | 45 | 81.25 |
| Unhealthy BP-5 | 55 | 46.875 |

Table IV
Performance of Back-propagation neural network with different tuning parameters such as the Weight vector W, Learning Rate $\eta$, and Percentage of training samples.

| % of training | Eta ($\eta$) | Weight set | Iterations | Prediction rate% |
|---|---|---|---|---|
| 50% (16 samples) | 0.1 | $W_1$ | 3723 | 71.875 |
| | | $W_2$ | 4109 | 71.875 |
| | | $W_3$ | 4019 | 68.75 |
| | 0.5 | $W_1$ | 2439 | 62.5 |
| | | $W_2$ | 3880 | 71.875 |
| | | $W_3$ | 3234 | 71.875 |
| 100% (32 samples) | 0.1 | $W_1$ | 6542 | 100 |
| | | $W_2$ | 248916 | 100 |
| | | $W_3$ | 532589 | 100 |
| | 0.5 | $W_1$ | 42518 | 100 |
| | | $W_2$ | 34291 | 100 |
| | | $W_3$ | 13262 | 100 |

## X. DISCUSSION OF RESULTS AND CONCLUSIONS

In 1906, a German physician Alois Alzheimer discovered the condition known today as Alzheimer's Disease. He noticed a recurring phenomenon in his patients. Often, they had difficulty understanding questions, confused, presented no signs of decision – making capabilities, and reasoning capabilities. When he performed autopsies on the patients, he noticed that there was an accumulation of certain plaques around the nerve cells, occurring in almost all of his cases. Neuronal degeneration and decreased connectivity were the pathophysiological hallmarks of the neurodegenerative illness.

This project introduced a novel technique in assessing a way to improve neural synaptic promoters in patients with Alzheimer's Disease. This was achieved by utilizing an artificial neural network which emulates information processing within the brain. By detecting the best learning (neuron design, how neurons interact) mechanism we were able to detect areas where connectivity will be strong. We also degraded certain neuron designs by altering information weights that **emulated information processing within Alzheimer's patients**. This is important because previous studies and research tried to improve neural synaptic connectivity in healthy networks, while this project tried to improve neural synaptic connectivity in unhealthy (Alzheimer's) networks.

We were able to come up with the following conclusions that are very vital in the future study of curing Alzheimer's disease:

- ***In prediction accuracy, the Back – Propagation Learning Architecture gave a 100 percent prediction accuracy (healthy network***
- ***The Perceptron Learning Architecture gave a 80 percent prediction accuracy (in producing a healthy network)***
- ***If we decreased the number of data given to the computer the prediction accuracy goes down***
- ***As the learning rate decreases the network takes more time to process information***
- ***Back – Propagation was the only network architecture that had 100 percent prediction accuracy***
- ***In our process of degradation of BP network, 40 - 45 weights needed to be spoiled in lowering the prediction accuracy This means that BP is the most efficient learning network.***

These results solidified our hypothesis that back-propagation learning mechanisms were the best network in improving unhealthy networks prediction accuracy. This statement is validated by the fact that our experimental results told was that over 40 weights was needed to be changed in order to decrease the prediction accuracy. In the future we plan to use clinical data of Alzheimer's patients and input this data into our established networks. The results of this investigation will be to validate our networks with clinical data from Alzheimer's patients.

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