Bio-sensored Diagnostic Kit for Detecting Tuberculosis Using Artificial Intelligence Through Neural Networks

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Abstract

The advancement and well-developed technologies in global medical field, tuberculosis remains a major health problem. To solve the problem of tuberculosis, artificial intelligence (AI) provides the way for solving problem in real world and enlightens the world in bringing a human's brain to a machine. This paper aims to detect the presence of mycobacterium tuberculosis infection within a short span of time compared to ancient technique. It is designed in such a way that the breath of the infected person can be used to diagnose the disease at premier stage. The main objective is to design and implement a portable diagnostic kit for Tuberculosis using Neural Networks and Artificial Intelligence. The tool kit called Electronic Nose which is significant artificial intelligent component constructed through neural network contains a biosensor having an electrode coated with the galectin. The signals of hybridization on binding will be captured and processed by machine learning sensor and the output is displayed using artificial intelligence. Earlier case of diagnosis approached on the basis of grouping microorganisms days together. But this study faster to find the report in an hour. Therefore the time taken for diagnosing the presence of the bacterium can be reduced and this also paves the way for starting the treatment immediately.

1. Introduction

One of the disease that has more infectious value is Tuberculosis (TB) which is initiated by multiple drain of Mycobacterium tuberculosis referred as Mycobacteria. Mycobacterium tuberculosis shows branching and resembling fungal mycelium in filamentous forms are rods of slender. It is an acid fast bacilli, which can form acid-stable complexes. The infectious cause are open for tuberculosis (lungs) of pulmonary. The approach of transfer of mycobacterium is through inhaling directly of bacilli is aerosolized in nuclei of sputum, sneeze, cough, transmission of respiratory fluids through the air etc. Nuclei in form of Droplet are projected for coughing in the air which comprise tubercle of bacilli. Approximately one cough releases 3000 droplets of nuclei and one time of sneeze release 10,000 droplets of nuclei. This affected active produces TB in others. Since from ancient days, a most important health problem Sis tuberculosis among millions of people. Today, tuberculosis kills 3 persons per minute worldwide. After the immunodeficiency virus in human the second trending disease is tuberculosis which cause high death rate. In 2013 they were 9 million cases of Tuberculosis and death rate is 1.5 million. At the end of 2014 almost 12.3 million cases are of positive Tuberculosis and 1,50,000 cases are type of multidrug resistant and was treated by programs of Global fund[1]. And so on. Finally at last in 2017, they were 2.790 million cases of Tuberculosis positive totally were found and been produced by WHO. The statistics of TB cases notified till 2017 is provided in Table 1.

Table 1
Reported of Tuberculosis cases

Year	Population of India covered under RNTCP	Total Tuberculosis cases reported	Total positive Tuberculosis cases reported	New positive Tuberculosis cases reported	Total negative Tuberculosis cases reported	New extra pulmonary Tuberculosis cases reported	Retreatment cases reported
2005	1,042,000,000	1,294,550	676,542	507,089	392,679	170,783	224,630
2006	1,112,000,000	1,400,340	746,149	554,914	401,384	183,719	260,618
2007	1,128,000,000	1,474,605	790,463	592,262	398,707	206,701	276,936
2008	1,148,000,000	1,517,363	815,254	616,027	390,260	220,185	289,222
2009	1,164,000,000	1,533,309	825,397	624,617	384,113	233,026	289,756
2010	1,177,000,000	1,522,147	831,429	630,165	366,381	231,121	292,972
2011	1,210,000,000	1,515,872	844,920	642,321	340,203	226,965	304,431
….	……..	…..	……	…….	…….	…….	…….
2017	2,560,000,000	2,790,000	1,320,336	1,021,000	584,321	360,446	401,468

In Indian population more than 40% of people were affected with Tuberculosis. In India, According to World Health Organization (WHO) about 3,00,000 people die by the cause of Tuberculosis[2].

All these data helps us to understand and find new technology to prevent and cure TB. Humanity of TB is too large because people are not access to diagnosis of healthcare and apt treatment is not provided. Measuring the cases of Tuberculosis is a long tie process which involves high cost and experiments for national level. Reporting to cases of Tuberculosis deliver a high deputation for the occurrence of TB which has performance rate high for the system to investigate.

By detecting tuberculosis at early stage and providing treatment it does not only remedy to that patient but also decrease the spread of disease in public. The laboratory diagnosis includes collecting specimen such as models of sputum which is collected on 3 continuous days in a container and kept for number of days to identify TB for pulmonary tuberculosis, urine samples are collected between 3–6 in the morning for renal tuberculosis, polymerase chain reaction, Target amplification, direct identification of Mycobacteria from DNA and RNA gene probes, etc will take lot of time to detect the presence of mycobacterium tuberculosis. Thus, to detect mycobacterium tuberculosis a novel strategy through neural network is used.

Neural network is also said as Artificial Neural Network (ANN) which is defined as an architecture is demonstrated after the brain. ANN is admired by one of the nervous system belongs to biological namely brain which is information processing paradigm. ANN is comprised of multiple number of neurons which are most highly consistent for problem solving which works in unity. A signal is send from node is the simple form of sample of real neuron that receives an input signal which is strong from the node to which it need to be connected.

Generally neural networks are a form of non-symbolic artificial intelligence is used for the manipulation of the output obtained from the learning paradigm of the neurons of the neural network. Neural models when observed through AI, gets models of complex mathematics with the output of floating point value to a machine with output of binary value.

The real time observation says when a person is affected by tuberculosis; the whole immune system gets destroyed, which paves way for the reception of all the disease. The only solution that could be made is to increase the speed of diagnosis. By increasing the speed of diagnosis, the accumulation of the disease could be prevented. Thus, inorder to make the diagnosis quite simple and easy, the method of ligand binding with the involvement of sensors can be implemented.

2. Current Scenario Of Tuberculosis

Tuberculosis involves the requirement of analysis in rapid manner to avoid from further spread and can permit for the management of its treatment. At present for diagnosing tuberculosis is slow process and are high cost.

The credentials of lipids utilizing a gas named chromatography-electron influence mass spectrometry (GC-EI/MS) will give the result. This test could be completed with the assistance of sputum tests. At the point when applied to an underlying arrangement of 40 sputum, interpretable outcomes were gotten for 35 examples with an affectability comparative with culture of 94% (95%CI: 69.2,100) and an explicitness of 100% (95%CI: 78.1,100). Be that as it may, blinded testing of a bigger arrangement of 395 sputum found the examine to have an affectability of 61.3% (95%CI: 54.9,67.3) and an explicitness of 70.6% (95%CI: 62.3,77.8) when contrasted with culture. Utilizing the outcomes acquired we built up an improved arrangement of order models, which when applied in a blinded re-investigation expanded the affectability and particularity of the measure to 64.9% (95%CI: 58.6, 70.8) and 76.2% (95%CI: 68.2,82.8) separately. Exceptionally factor levels of foundation signal were seen from singular sputum tests that repressed understanding of the information. These example preparing are required to upgrade the affectability and power of the test.

A reaction for analysis of tuberculosis was estimated with 60 specimens of fixed formalin tissue using polymerase chain reaction. The major utensils are sputum with stained smear and culture and radiography in chest for the identification of tuberculosis by the clinics. The tests could be carried out using two methods, DNA Amplification and Tissue processing.

By use of dispensable, positive dislodging pipettes, 5 µl of the DNA remove from each example was added to 50 µl of a PCR response blend containing 10 mMTris-HCl; 50 mMKCl; 3.75 mM MgCl2; 0.18 mM every one of deoxyadenosine triphosphate (dATP), deoxycytosine triphosphate (dCTP), deoxyguanosine triphosphate (dGTP), and deoxyuridine triphosphate (dUTP); 0.001% gelatin, 0.68 mg/ml acetylated ox-like serum egg whites (BSA); 1,000 duplicates of a formerly portrayed inward control DNA succession ; 1 U of Taq DNA polymerase; and 0.18 µm of preliminaries T4 and T5.

For diagnosing tuberculosis Elisa test is used by utilizing purified Antigen A60 which is removed from mycobacterium. It is applied for sensitivity and specificity with 95%. The antibodies like IgG and IgM are separately tested. IgM of antibodies are able to diagnosis quickly and IgG are diagnosed later. Test result is healthy and normal and has no significance of BCG vaccine and tuberculin test. Antigen A60 is a communal for all mycobacterial like tuberculosis, leprae, bovis and avium. Along with the outcome of Elisa test other laboratory result like clinical, radiology and etc. must be compared for final stage of diagnosis.

By studied all the above, the issues involved in finding tuberculosis are

1. The process like gas chromatography and mass spectrometer takes sputum for discovery of tuberculosis. The most of the available methods involve diagnosing with blood samples.
2. The current diagnostic methods take duration in terms of days and hours for confirming the presence of the disease. As the disease is diagnosed with a time delay there could be a chance for getting it spreaded to others. Also these methods are costly to affordable to all the people.

To solve the above problem such as time taken for finding the presence of tuberculosis and spreading of disease, this paper proposes a portable diagnostic kit for tuberculosis using neural networks and artificial intelligence.

3. Literature Survey

The Detection Kit named Genedia MTB/NTM is one of PCR multiplex analyze kit utilized in the process of identification differential Mycobacterium tuberculosis complex (MTBC) and nontuberculous mycobacteria (NTM). This is recognized as that data is limited on the recital of kit analyze to date. Totally 687 successive sputum samples are refined and analyzed with the kit. Nineteen specimens are positive in MTBC and 69 (10.0%) are positive for NTM based on the culture. Every samples displayed outcomes for MTBC using both investigations. The suggestion between positive NTM by utilizing genedia MTB/NTM and the analysis of NTM respiratory syndrome are not significant. The PCR assays showed analytical routine for MTBC detection [21].

The routine of Kit VereMTBTM for identifying multidrug resistant tuberculosis (MDR-TB) is authenticated for 124 sputum models. For comparing along with culture of MGIT, specificity and sensitivity of the Kit VereMTB to perceive MTBC are 97.0% and 98.3%, respectively. Compared with MGIT DST, the sensitivity and specificity of Kit VereMTB to RIF's detecting the resistance are 85.7% and 93.9% respectively, and the sensitivity and specificity of Kit VereMTB for INH resistance identification are 75.0% and 95.7%, respectively. 6 models of NTM were identified correctly. The Kit VereMTB identifies MDR TB quickly and precisely in models of sputum [22].

For analysis of tuberculosis conventional method like culture and smear are considered. The diameter cell ranges between 0.3 µm and 0.5 µm and also grouped under rod shaped bacilli. This growth rate of this bacteria is slow and are divided into group like positive gram and acid type with fast bacillus [13].

The symptoms of tuberculosis are pain in chest, cough for more than 3–4 weeks, high fever and sweat at night, loss of weight, pallor and fatigue. When the infected person sneeze or cough then the healthier person is affected with tuberculosis [9].The bacteria in tuberculosis consists of cell wall with thick layer of acids called mycolic [6].

The method called six-minute with point of care and breath test for breast cancer is examined for volatile Biomarker in women [1]. Leave-one-out procedure and Multivariate predictive algorithms were employed to identify significant biomarkers with multiple Monte Carlo simulations and cross validated. Screening process was done for normal healthy women and abnormal women to test the performance.

The analyses smear type of sputum requires extremely skilled employee are avoided for extreme mistakes. Here, preprocessing such as symmetrical structures of cell image are extracted in the form of binary image consists of compactness, circularity, tortuosity and eccentricity are inputs to the backpropagation in neural network. Authors were accomplished 100 samples in which training are 75 and testing are 25 samples. After training, classifier finds the TB bacteria with 2 labels: TB bacteria yes else TB bacteria not. Author proved the result with the accuracy mean square error of 0.000368[2].

Jaramillo emphasis the need to develop a system that is capable of detecting tuberculosis-related biomarkers that can provide a quick diagnosis to begin treatment immediately. The Development of piezoelectric immune sensor for rapid and efficient tuberculosis detection was obtained as potential bio-receptors. The obtained immune reagents will be used as specific recognition bioactive molecules, in combination with functionalized quartz crystals, to build a piezoelectric immune sensor for the detection of Mycobacterium tuberculosis biomarkers, which can be related to the disease [4].

Osman, M.K suggested that the manual screening of finding disease is time consuming, laborious and tedious process. In this paper a technique of image processing and automated intelligent with neural network method is used for separation and identification of bacilli with tuberculosis detection in tissue section. Three steps were followed in this paper such as In Ziehl-Neelsen staining approach after satin image are taken for bacilli for samples and cluster method like K-means is used for extracting tissue and bacilli of tuberculosis and at last features with geometric are considered. This paper experimentally produced result with is more effective and precise to identify the bacilli with tuberculosis in the tissue [5].

Osman suggested that multiple approaches are utilized for the identification of tissue with tuberculosis and restrictions of present method is utilized to detect tuberculosis. Here, to speed up and simplify the analysis process of mycobacterium TB, a non-invasive technique founded were the belongings of electrical are projected.

4. Materials And Methods

The projected system is utilized for diagnosing tuberculosis within short period. It takes the breath from the human beings, and detects it through the biosensors. The output obtained from the biosensors are too small in amount, hence the neural networks is used to process the output. The processing units (nodes or neurons) of the neural networks work in unison to take the signals from the cations and anions liberated from the sensors when the corresponding bacterium reacts with the binding protein. The feed forward network is used for taking feed from the biosensors. Then the output is displayed using AI.

5. Analyzing The Working Of Neurons

In this there are two modes of operations of neurons-

1. **Training Modes**: For particular pattern of Input, the neuron are trained to fire or not
2. **Utilizing Modes**: When a pattern for training mode is identified, then its associate result becomes present output.

Steps involved in confirming tuberculosis presence are

1. Rebiating the structure of galectin

2. Docking of Mycolic Acid
3. Interaction of two molecule output

5.1 Identifying the Structure of Mycobacterium Tuberculosis and Galectin

Identifying structure of the protein, namely Galectin 3 stays to be a great challenge. When the structure of both ligand and the protein is known, studying the interaction would become much easy. The structure galectin protein is available in the biological database (homology modelling of galectin). Thus it would be easy to retrieve the needed structure. Protein structure made of Amino acids. Thus to predict the structure of the Galectin protein, a technique called Homology Modelling were used. Homology modelling can be done by using licensed software called PRIME. We need python scripts to work with modeller. The scripts are readily available in the modeller. First step to do is, to obtain the protein sequence from the PDB. The protein sequence is made of various Amino acids. The various amino acids are represented by alphabets.

The protein sequence of Galectin is > P1; qseq1

Sequence: qseq1::::::: 0.00: 0.00

MADNFSLHDALSGSGNPNPQGWPGAWGNQPAGAGGYPGASYPGAYPGQAPPGAYPGQAPPGAYPGAPGAYPGAPAPGVYPGPPSGPGAYPSSGQPSATGAYPATGPYG

The obtained sequence is in the Protein Information perome format.

5.2 Docking of Mycolic acid and Protein Training ANN for Processing the Output

In Molecular modelling two methods are used for docking community with molecular. The first methods uses matching of technique which defines the ligands and protein with respect to surface and the second approach uses the technique of simulating docking method that energies relates for pairwise of protein ligand is evaluated and this docking technique for approach. Docking is a technique that examines and an obligatory for particle that to second is constrained to each other for complex. The strong point of association is expected for alignment of knowledge between particle example function scoring.

The association in between particle like proteins, carbohydrates, lipids and nucleic acid has a major part transduction of signal. Two followers of interrelating will affect the category of produced signal for example agonism vs antagonism in relative orientation. Docking is utilized for calculating both type of produced signal and strength. Docking also plays major part in drugs in process of rational design. The significance of biological and pharmaceutical of particle docking is taken with the effort of prediction toward improving the method.

The ligands and protein with set of features is described by geometric matching is used in the process of docking and the features comprises surface of complementary descriptor. The particle surface of the receptor is termed as accessible solvent area of surface and the ligand surface is termed as description of matching surface.

Thus it is planned to inhibit the docking process using the software called auto dock or patch dock. The name of the components used in the kit is electrode, transducer, amplifier, detector and binding compound is Galectin. It is developed under Mat lab with the integrated components such as Auto dock, Modeler, Ransom viewer.

6. Experimental Result And Discussion

Galectin from homosepians sequence was retrieved from NCBI lam pept (GI 413862) Acumou name in humgalbin binding protein mRNA. The gene name is Mac2. The gene sequence was then translated in to six forms translation method and generated possible forms. Further the sequence was combined and aligned for conservative identity. The translated sequence was subjected to predict structure using homology modeling.

Modeling was done using PRIME module from schodringer by taking two template as structure. The modeled structure was protected for quality check by procheck (Fig. 4.1.2). The quality of the protein was observed as 90% more than its library. So the protein is technically qualified to be an Histidine in biological form. Further the protein was considered to do energy mutation to get high energy constraints. The hierarchical portability to have the protein mass to energy should be minimum.

6.1 MAC2 Gene sequence as follows

>gi|413862|gb|M64303.1|HUMGALBIN Human galactoside-binding protein mRNA

GCAGCCACCGAGCGGAAAATGGCAGACAATTTTTCGCTCCATGATGCGTTATCTGGGTCTGGAAACCCAA
ACCCTCAAGGATGGCCTGGCGCATGGGGGAACCAGCCTGCTGGGGCAGGGGGCTACCCAGGGGCTTCCTA
TCCTGGGGCCTACCCCGGGCAGGCACCCCCAGGGGCTTATCCTGGACAGGCACCTCCAGGCGCCTACCAT
GGAGCACCTGGAGCTTATCCCGGAGCACCTGCACCTGGAGTCTACCCAGGGCCACCCAGCGGCCCTGGGG
CCTACCCATCTTCTGGACAGCCAAGTGCCCCCGGAGCCTACCCTGCCACTGGCCCCTATGGCGCCCCTGC
TGGGCCACTGATTGTGCCTTATAACCTGCCTTTGCCTGGGGGAGTGGTGCCTCGCATGCTGATAACAATT
CTGGGCACGGTGAAGCCCAATGCAAACAGAATTGCTTTAGATTTCCAAAGAGGGAATGATGTTGCCTTCC
ACTTTAACCCACGCTTCAATGAGAACAACAGGAGAGTCATTGTTTGCAATACAAAGCTGGATAATAACTG
GGGAAGGGAAGAAAGACAGTCGGTTTTCCCATTTGAAAGTGGGAAACCATTCAAAATACATGTACTGGTT
GAACCTGACCACTTCAAGGTTGCAGTGAATGATGCTCACTTGTTGCAGTACAATCATCGGGTTAAAAAAC
TCAATGAAATCAGAAAACTGGGAATTTCTGGTGACATAGACCTCACCAGTGCTTCATATACCATGATATA
ATCTGAAAGGGGCAGATTAAAAAAAAAAAAAAAGAATCTAAACCTTACATGTGTAAAGGTTTCATGTTCACTGTAGAGAAAATTTTTACATTCATCAATATCCCCCC

6.2 Translated Sequence and Protein Sequence are as follows

Translated Sequence:

QPPSGKWQTIFRSMMRYLGLETQTLKDGLAHGGTSLLGQGATQGLPILGPTPGRHPQGLILDRHLQAPTMEHLELIPEHLHLESTQGHPAALGPTHLLDSQVPPEPTLPLAPI

GGILMNVKIFSTVNMKPLHMGLDSFFFFLICPFQIISWYMKHWGLCHQKFPVFFHVFPDDCTATSEHHSLQPSGQVQPVHVFMVSHFQMGKPTVFLPFPSYYPALYCKQLSC

SSHRAENGRQFFAPCVIWVWKPKPSRMAWRMGEPACWGRGLPRGFLSWGLPRAGTPRGLSWTGTSRRLPWSTWSLSRSTCTWSLPRATQRPWGLPIFWTAKCPRSLPC

GGYMKFSLQTNLYTCKVILFFFFSAPFRLYHGISTGEVYVTRNSQFSDFIEFFNPMIVLQQVSIIHCNLEVVRFNQYMYFEWFPTFKWENRLSFFPSPVIIQLCIANNDSPVVLIEA

AATERKMADNFSLHDALSGSGNPNPQGWPGAWGNQPAGAGGYPGASYPGAYPGQAPPGAYPGQAPPGAYHGAPGAYPGAPAPGVYPGPPSGPGAYPSSGQPSAPGAYP

GDIDECKNFLYSEHETFTHVRFRFFFFFFNLPLSDYIMVYEALVRSMSPEIPSFLISLSFLTRLYCNKASFTATLKWSGSTSTCILNGFPLSNGKTDCLSSLPQLLSSFVLQTMTL

Protien Sequence:

> 1KJL:A|PDBID|CHAIN|SEQUENCE

GPYGAPAGPLIVPYNLPLPGGVVPRMLITILGTVKPNANRIALDFQRGNDVAFHFNPRFNENNRRVIVCNTKLDNNWGREERQSVFPFESGKPFKIQVLVEPDHFKVAVNDAHL

Mycolic acid structure was taken to moderate with galectin protein by slide method. The structure was analyzed to proceed functional annotation. It shows the occupancy has more number of hydroxyl and ethyl group.

Docking of Mycolic acid derivative with galectin protein was studied. The differential g score was identified from the galectin Mycolic acid complex − 8.06, -7.23, -5.85, -4.22, -4.56, -4.89, -5.99, -5.21, -4.28, -4.34 E(kj/mol). Finally α_1 derivative has − 8.06 g score having higher binding affinity towards galectin protein.

The initialization of NN is being done with the help of Matlab. Already trained templates would be available in the software, hence, easy access might be possible.

Type can be chosen by which the training of NN is done. Since this project used the fitting tool to train the NN.

The fitting tool is selected to study about the number of hidden layers and the output layer is made.

The formation of the hidden layers is obviously seen and the simulation is enhanced. The whole architecture is formed by fixing of hidden layers.

Once when the input gets loaded into the network, the process starts. The performance and various training states can be seen.

Thus the Output is obtained in the form of graph and various ranges of values are plotted successfully. The trained targets and test outputs are also displayed. This when practically implemented in a kit can be synthesized easily.

7. Conclusion And Future Work

One of the six senses i.e., smelling through electronic nose could be brought into the machine, thereby making the machine almost a human. The available methods for finding tuberculosis involves diagnosing with blood, but the proposed method will be painless since it does not involve blood samples This paper presents that these electronic noses are developed through neural networks, it is understandable that all the other five senses can be brought into the machine through neural networks. The existing methods make use of the separated components of the organism using modern analytical techniques which are too expensive. Comparatively, the diagnostic kit which is to be built will be cost effective and time reducing. In future, when the kit gets fully developed the whole diagnosis process can be highly advanced by making it efficient enough to detect the type of tuberculosis.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

ST and NMS designed the study, SL and KH implanted the work, AK and NK wrote the manuscript. All authors read and approved the final manuscript.

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Figures

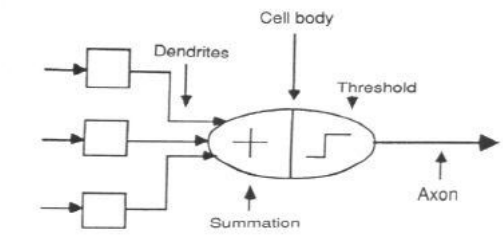

Figure 1

Artificial Neural Networks

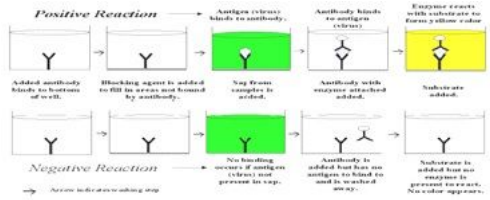

Figure 2

Steps involved in ELISA test

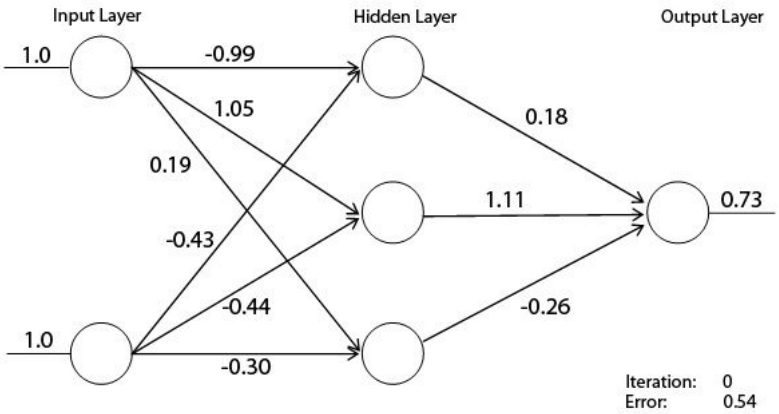

Figure 3

Example of weighted network

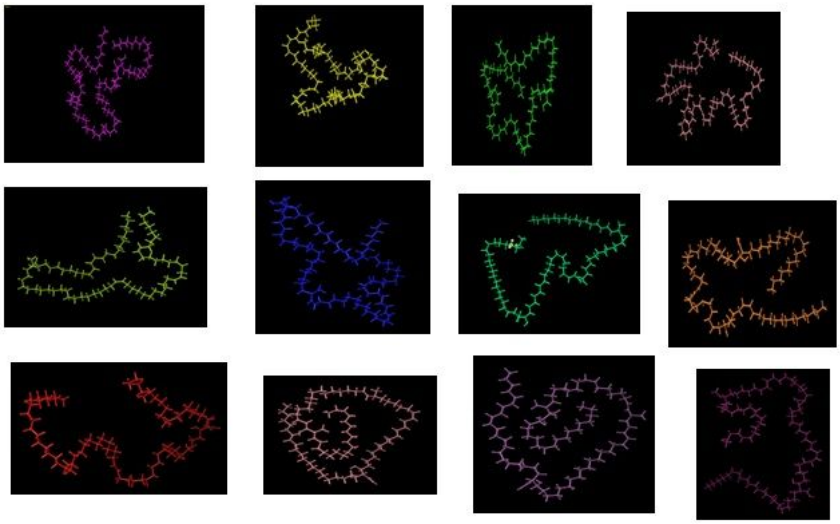

Figure 4

Different forms of Mycolic Acid

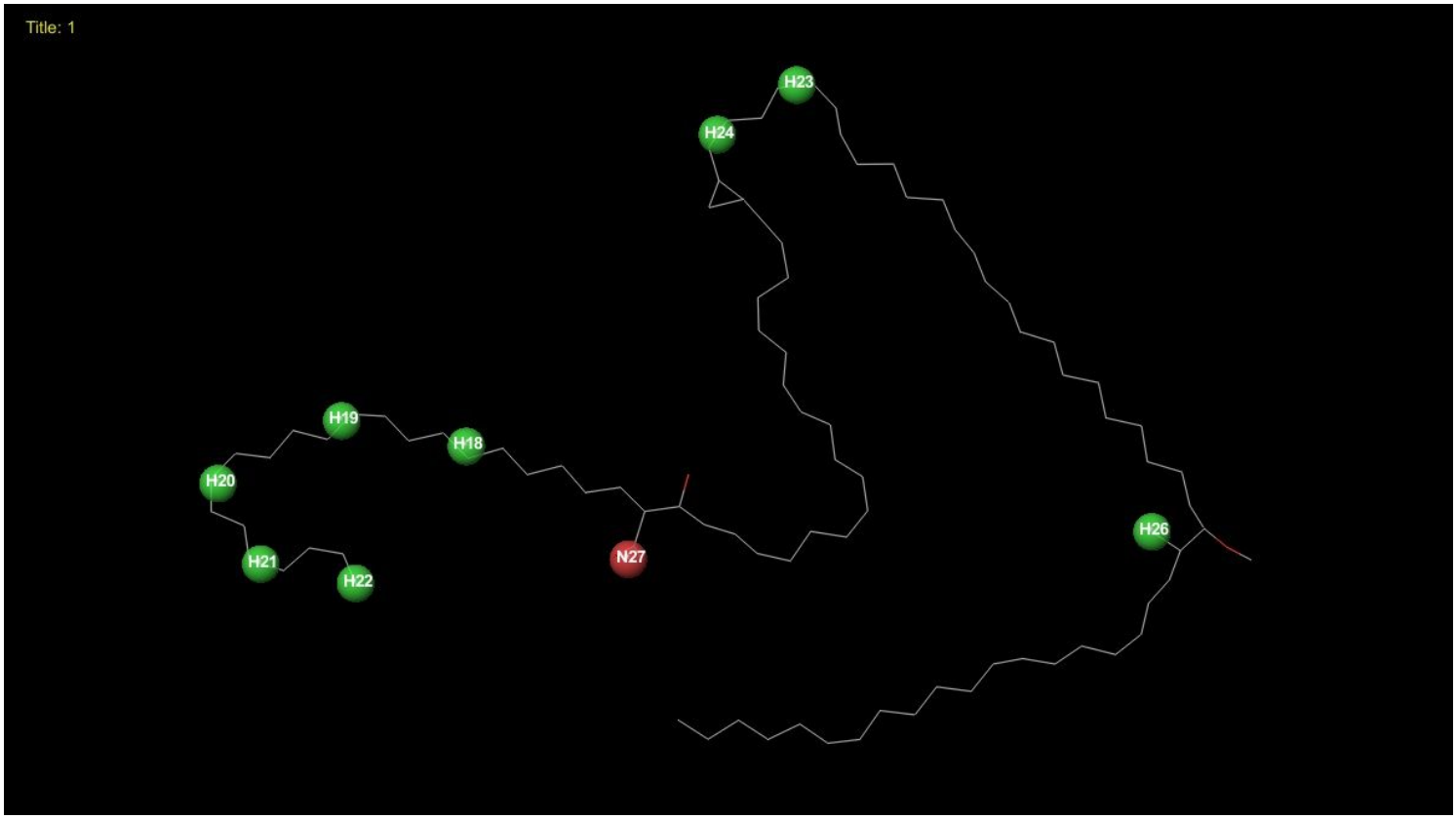

Figure 5

Pharmacophore comparisons for selected ligands

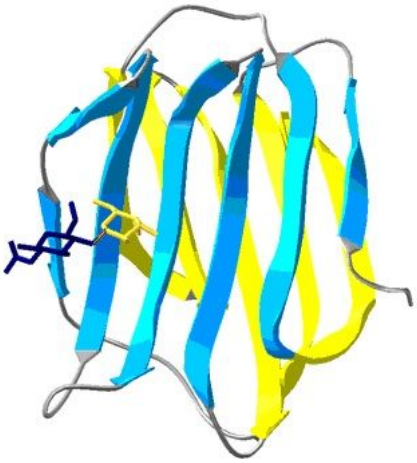

Figure 6

Structure of Galectin CDR

Figure 7

Translation frames

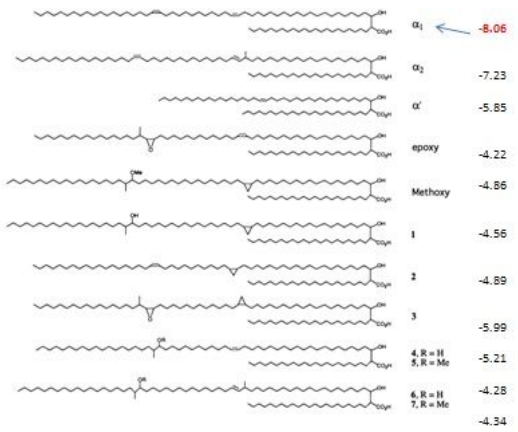

Figure 8

Slide Methods

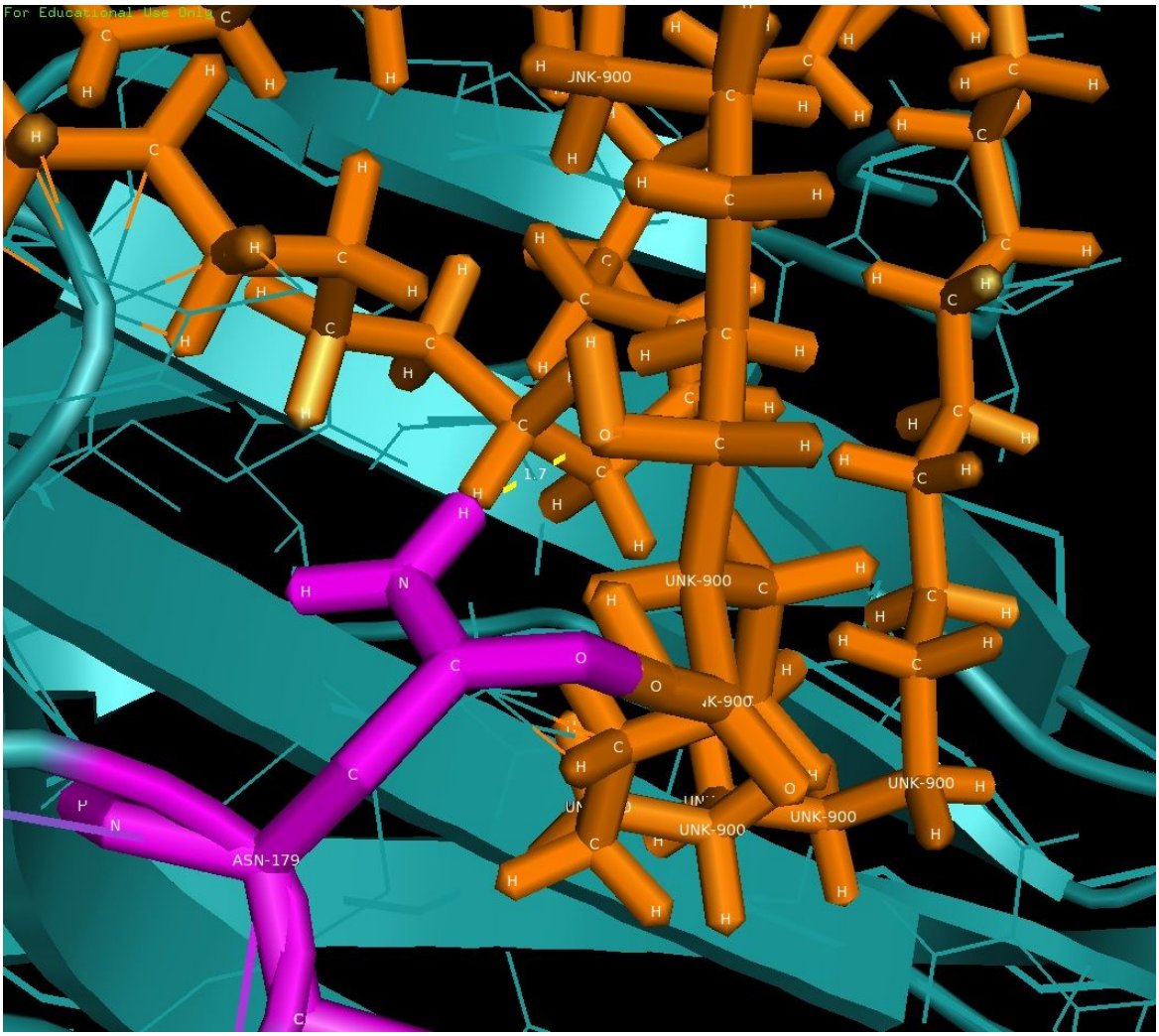

Figure 9

The Interaction of Mycolic Acid and Galectin

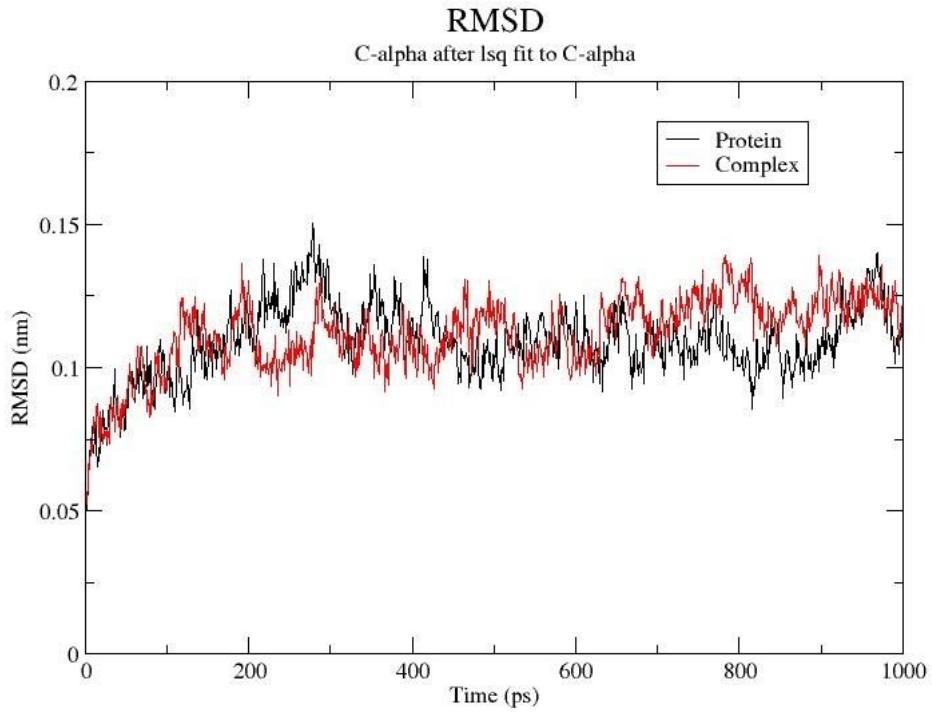

Figure 10

MD Simulation Results- RMSD Graph

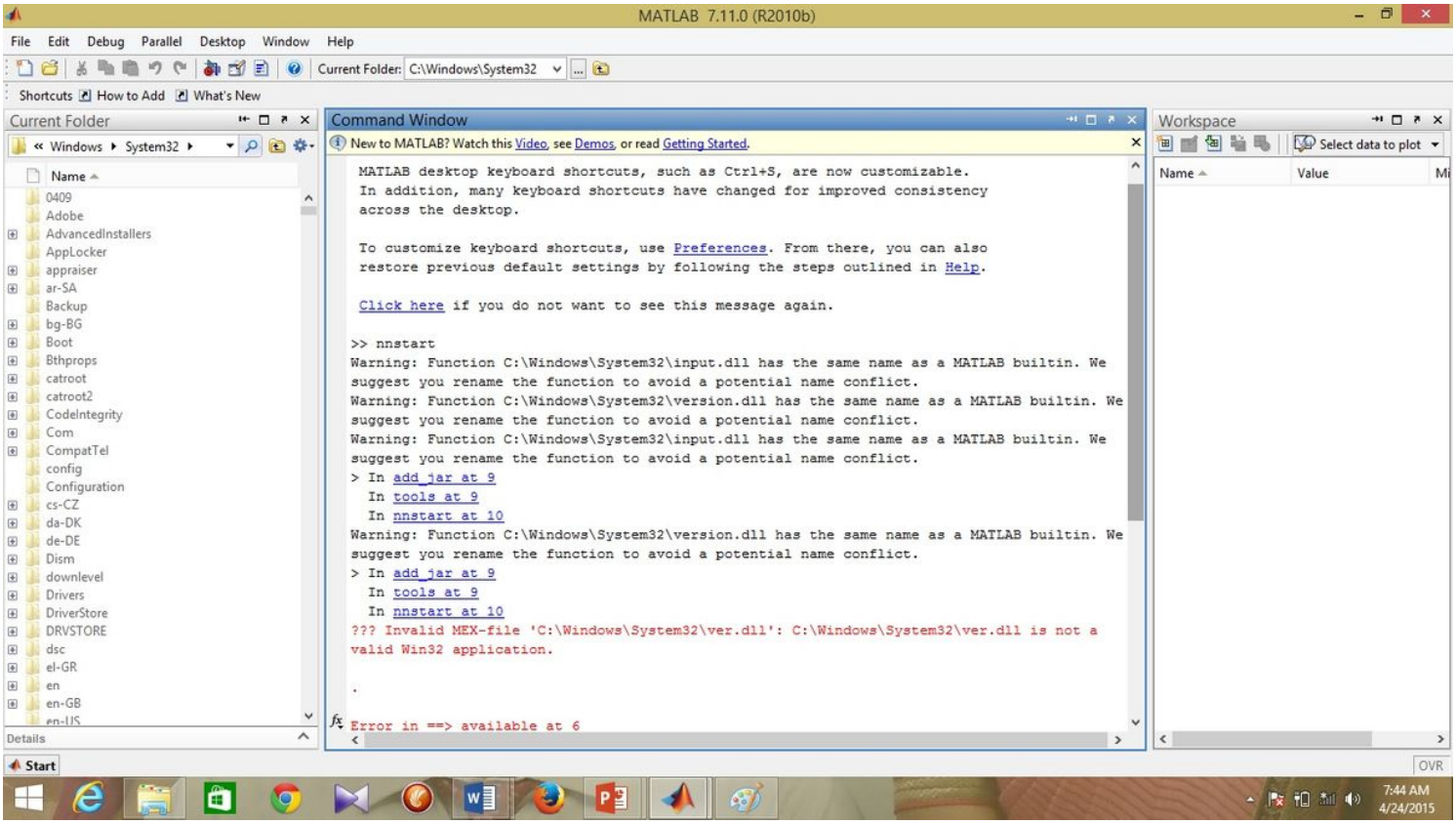

Figure 11

A1: Starting the Neural Network

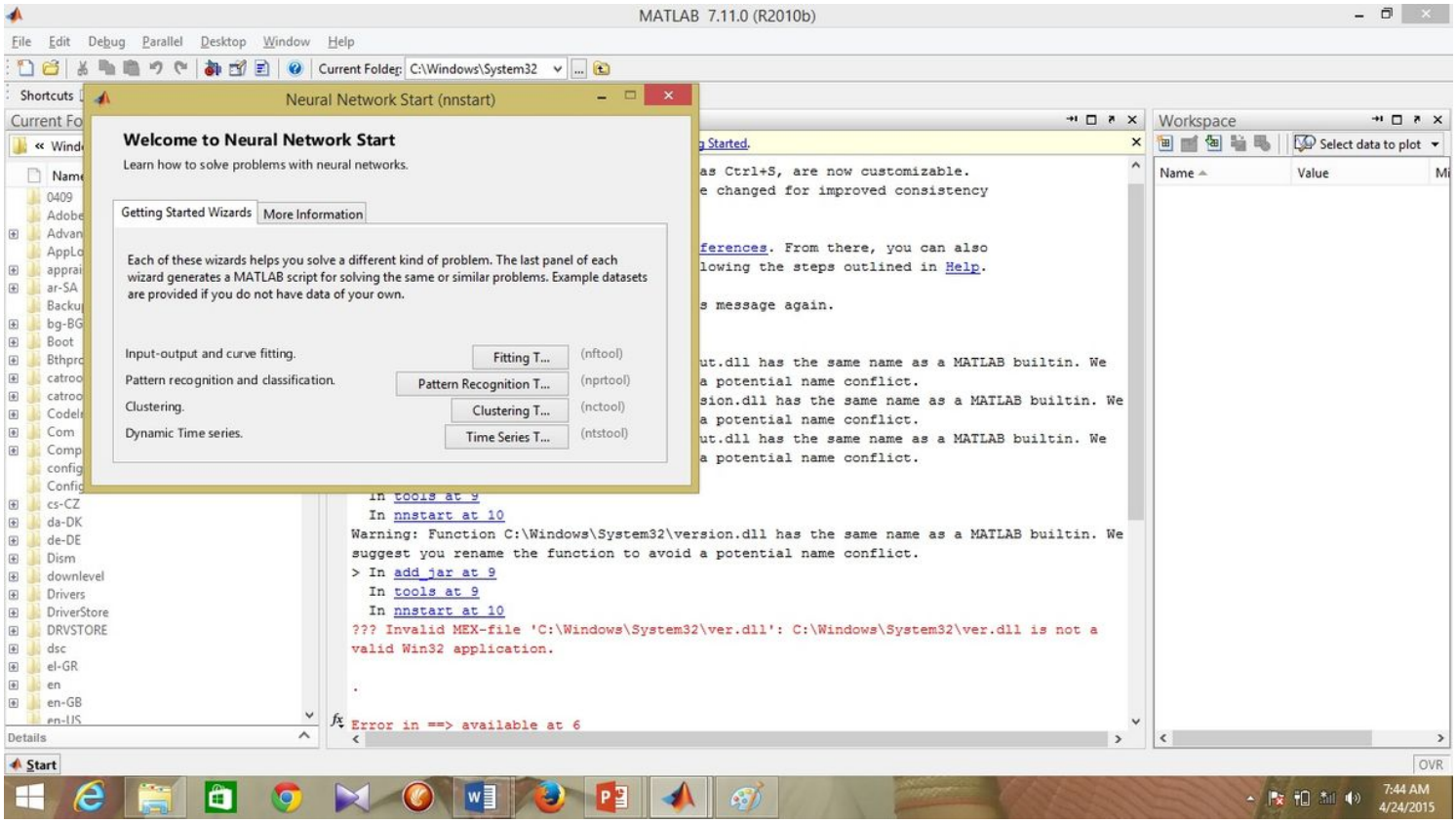

Figure 12

A2: Selection of Type of Training in NN

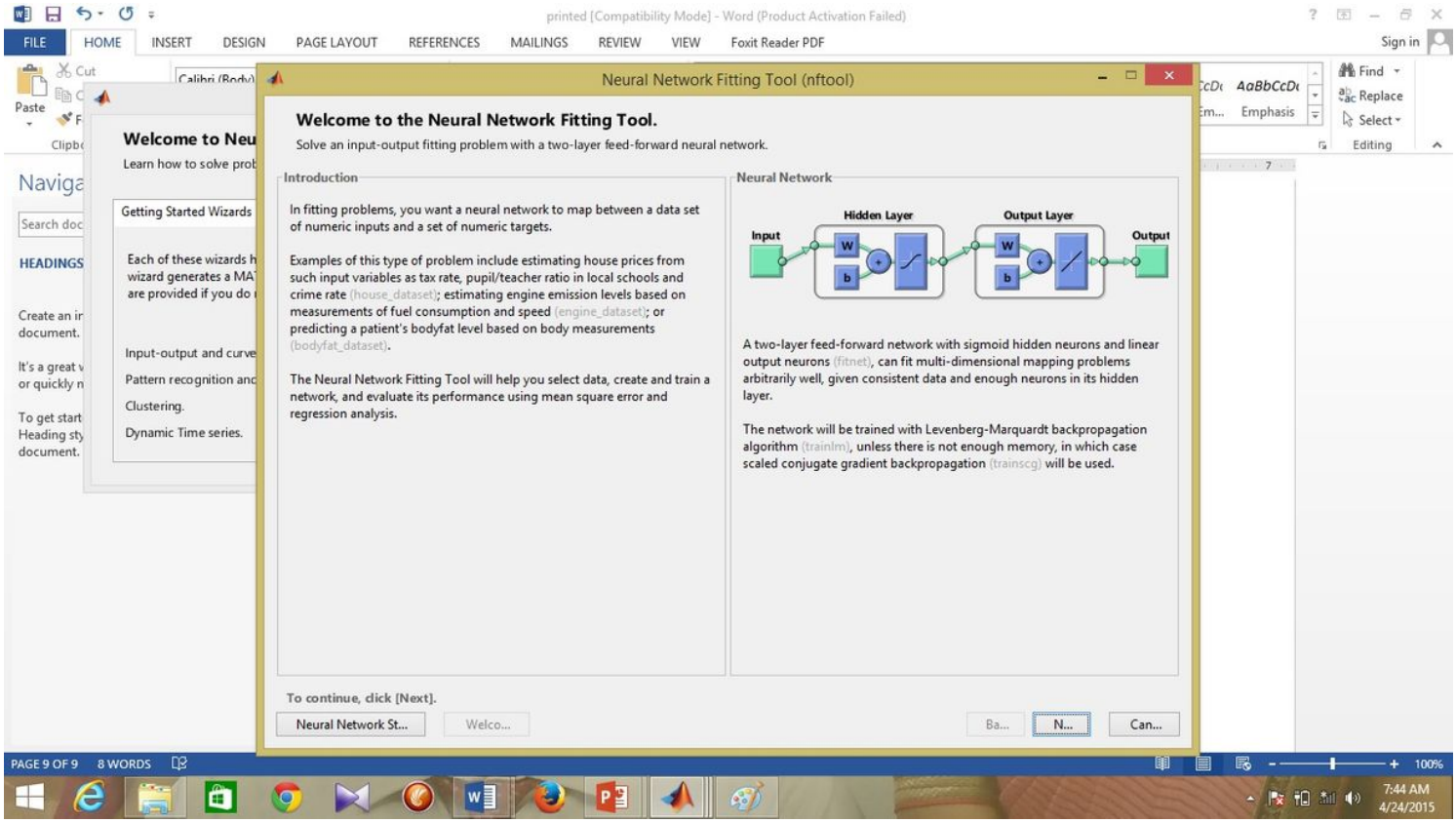

Figure 13

A3: The fitting Tool Selection

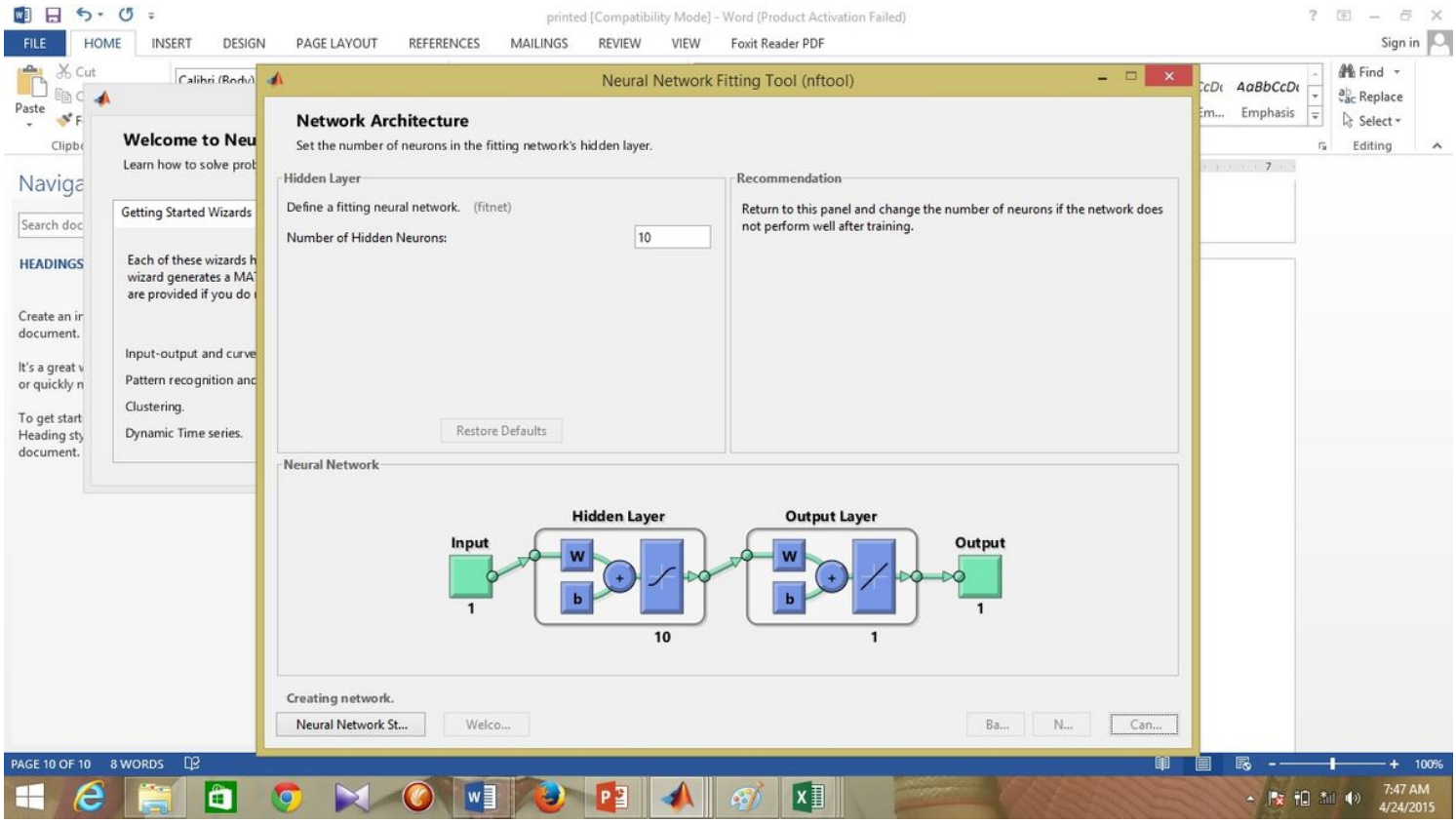

Figure 14

A4: The hidden layer Formation

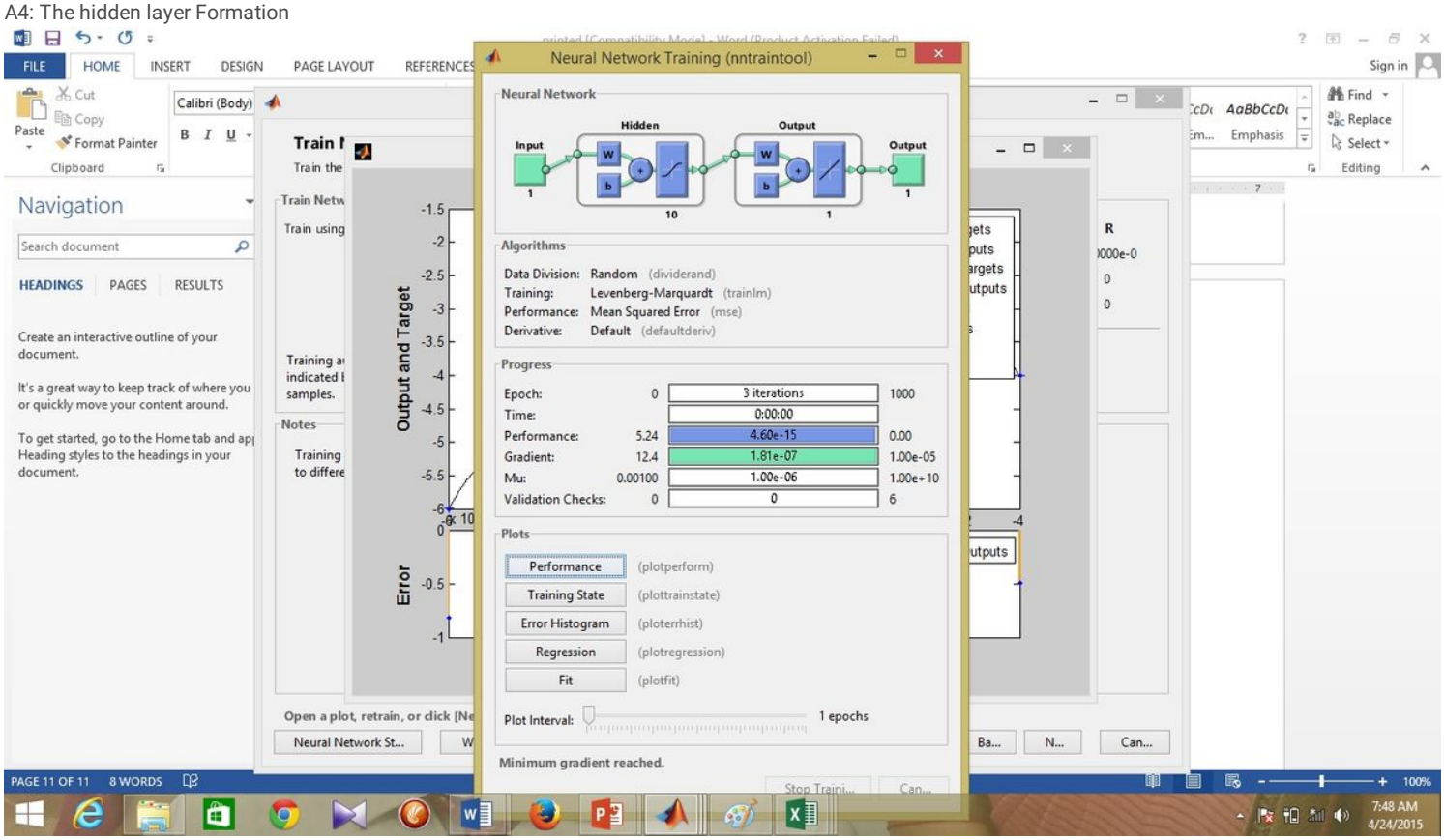

Figure 15

A5: The performance strategy is obtained

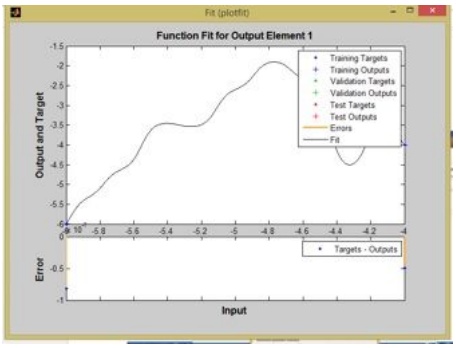

Figure 16

A6: Output for Trained Targets