

Simulation Based on Neural Network Architecture Reference On Nano-bio Sensors Model for Cancer Diagnosis and Automated Drug Delivery System With MATLAB

Shahla.Hasanzadeh¹, Meraj.Rajae²

1- Department of Electrical Engineering, Shariaty University, Tehran, Iran

Email: sh.hasanzadeh@yahoo.com

2- Department of Electrical Engineering, Teacher of Shariaty University , Tehran, Iran

Email: meraj.ra@gmail.com

Received: November 2014

Revised: December 2014

Accepted: February 2015

ABSTRACT

In this paper, a mathematical model is required to describe the nanowires and nanodevices by software is Designing , modeled and implemented . In graphs obtained from the simulation of neural network based on its model reference nano-sensorsm ,the current during the reaction and the surface concentration of corresponding tumor cells , identical to the obtained graphs from the test setup, is obtained that based on, a mathematical model based on MATLAB for nanodevices developed and in Designing a nano-bio sensors are used to detect disease. Arrays reference model in this paper consists of 64 nanowire sensor that it 's used to detect prostate cancer. In this paper, a modified method based on principal component analysis (PCA) and neural network design is presented when compared to other existing methods that have almost accuracy 94%, the highest accuracy correctly of 99.28% is capable.

KEYWORDS: Nano-bio sensors, Neural networks, Nanowires, Sensor Modeling, Analyte concentration, Voltage - Current diagram, Disease Detection.

1. INTRODUCTION

There are currently a large number of nano- biosensors for medical applications can be used in diagnosis. In developing a system for diagnosing diseases, modeling software is one of the core requirements. MATLAB software environment which is primarily used to develop software reference model. Various sensor models are available in current MATLAB built-in, easy to develop mechanical systems Ref. [1]-[2]-[3]-[6]-[10]-[11]. In this work, we develop to explain a mathematical model for nanowires that are used to detect cancers. Three different sensor models based on the results of techniques curve fitting methods Sensor model developed to generalize the use of Savitzky-Golay Filter (SG filter) is passed. The modeled sensor can be used for automated drug delivery and diagnostic devices. The sensor array consists of 64 models nanowires and nanowire sensors in the 8×8 matrix using a Gaussian distribution function can be distributed. The new array sensor consists of a flat sensor and nanowire sensors may be used to increase the sensitivity of detection of prostate cancer occur in the system. A leading path detection system based on neural network architecture.The network design consisted of two layers of sigmoid transfer function and performance purelin (linear). The ideal weight for layer

are identified using back propagation algorithm Levenberg-Marquardt (LM). The method of linear discriminant analysis (LDA) and principal component analysis (PCA) is incorporated into an expert system that can extract important features of cancer cells based on the classification. A Proportional derivative - Integral (PID) controller may be modeled to control the diffusion pump and monitoring of drug diffusion. PID controller output detection system should also lead to the release of the drug. Field Parts programmable gate array (FPGA) have been designed and developed to implement the architecture of neural networks and PID controller optimized for area, speed and power performance. Development model for nanowire sensors is matching with sensor models are available with a standard deviation of less than 2%. Prostate specific antigen (PSA) antibodies and deoxyribonucleic acid (DNA) as biomarkers for prostate cancer detection based on sensor array has been constructed. The sensor array to achieve approximately 99% efficiency and the error is only 1% compared with existing design is created. the Decision Generated by the system to identify drivers PID controller to activate the pump release PID controller with error less than 12% suppression time is less than 10ms. For real-time detection and recognition system developed is

incorporated into a true bio-chip.

2. DNA SENSORS

Human genome (DNA sequence that is unique and known) has billions of DNA base domains for DNA sequencing is feeling. Sensor arrays are used to measure genome. Bio-nano-sensor arrays of sets of X-Y elements. This pixels is composed more of elements that called electronic components Ref. [4]. Each parts of a sensor can be a nanowire transistors, carbon nanotubes, planar transistor, etc. Each element, a genome is connected to the sensor. The molecules connected the source-drain determine of target Sensors and current to flow between the source and drain. The sensitivity of the sensor to a mol up to micro mol is estimated (10^{-6} (M)) Ref. [5]. This value is very small, so it is essential that the sensor be more sensitive for the diagnosis. To improve the sensitivity of a sensor for biological applications, carbon nanotubes (CNT) are introduced. CNT sensor sensitivity compared to nanosensore, though characterized by their size, compactness femto 10^{-15} (mM) increases for biomedical applications. Figure 1 show the DNA sequence of a set of sensors and sensor connected.

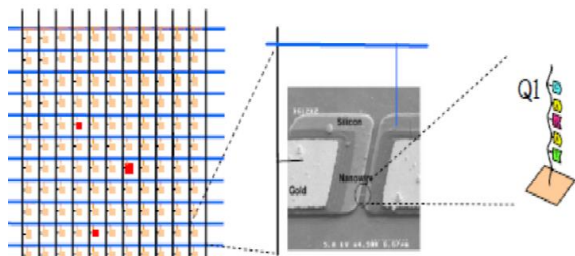


Fig.1. Nanosensor array and DNA sensor Ref. [5]

The sensor is composed of multiple receivers. Unknown molecule, only the sequence of unknown molecules are conjugated to the receptor sequence, the target molecule is absorbed by the receptors and their propagation occurs along the surface receptors. And the necessary to create a relationship between the number of molecules detected And Create Streaming in the time it takes to detect and determine the concentration of molecules. Equation absorption - emission Ref. [9]-[8]-[7] to understand the behavior of the sensor needs to be analyzed. The analysis of the number of molecules adsorbed in the Equation (1) is given. This is the journal Imanager, have been published. Ref. [12]

$$N(t) = \rho_0 t \left[\frac{A}{C_0} + \frac{l}{k_F N_0} \right]^{-1} \quad (1)$$

3. REVIEWS CHARACTERISTICS OF THE SENSOR

Based on the Discussed mathematical model, nano-bio-sensor available tool to simulate ISFET to the central

organization, nanowires and nano-spheres are used. One of the most important parameters required for biological sensors include:

- Size of micro channel: $5(\text{mm}) \times 0.5(\text{mm}) \times 50(\mu\text{m})$
- Flow rate of fluid in the channel: 0.15ml/h
- Concentration of antigens in fluid: $2 \cdot 10^{-15} \times 6 \cdot 10^{23} \approx 10^9$
- Number of antigens through channel per hour: $1.5 \times 10^{-4} \times 10^9 \sim 10^5$ (~ 42 per second)
- Total area occupied by Antibodies: $5(\text{mm}) \times 0.5(\text{mm}) \sim 25 \times 10^{-7} (\text{m}^2)$
- Area of one Si NW occupied by Antibodies (Assumption: $r \sim 10(\text{nm})$, $l \sim 2\mu\text{m}$): $2\pi r l \sim 1.26 \times 10^{-15} (\text{m}^2)$
- Target receptor conjugation
- Type of antigen: DNA
- Ratio between total occupied area and Si NW: 2×10^9
- Mean time between one antigen reacts with one antibody on the Si NW: <3 minutes

Based on the above parameters, the parameters of biological sensors have been developed in the laboratory and in the laboratory model of the sensor, are simulated. The design parameters of nanodevices, the ultimate goal of the experimental setup to determine the response time of the sensor, analyte concentration and receptor density is married.

4. THE CHARACTERISTICS OF SILICON NANOWIRE AND EXPERIMENTAL SETUP

A silicon nanowire is developed with the following parameters, the VI characteristics of the nanowire is simulated using the biosensor tool. Sensor parameters: Diameter of silicon nanowire: $10(\text{nm})$, Oxide thickness: $5(\text{nm})$, Gate length: $50(\text{nm})$, Channel doping: $1 (e+21 / \text{cm}^3)$. Analyte concentration parameter is varied from 0.1 to $1 (\text{nmol/L})$, corresponding changes drain current in the nanowire sensor is determined. Figure 2 shows the graph of concentration vs. device current characteristics for nanowire sensors.

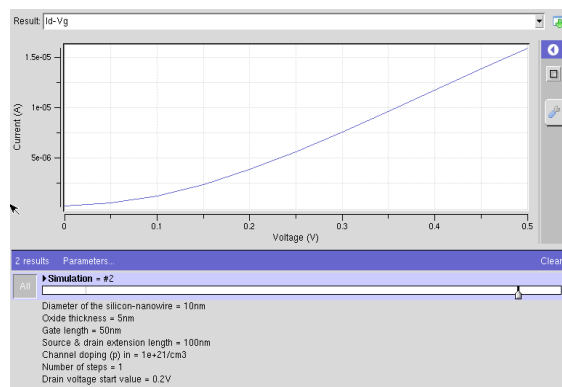


Fig.2. Concentration vs. device current

Table 1 shows currents and concentration in terms of the sensor voltages, for three different sets of steps. Simulation results using MATLAB are obtained.

Table 1. Currents and corresponding concentrations of sensors

Concentration in (nmol/L)	Sensor current Equivalents(nA)	Concentration In(nmol/L)	Sensor current Equivalents(nA)	Concentration In(nmol/L)	Sensor current Equivalents(nA)
0.1138	0.2049	0.0604	0.1088	0.0907	0.1633
0.1723	0.3101	0.0826	0.1487	0.1055	0.1899
0.1768	0.3183	0.1099	0.1978	0.1192	0.2146
0.2002	0.3604	0.1137	0.2046	0.124	0.2232
0.2336	0.4205	0.116	0.2088	0.1297	0.2335
0.2772	0.4989	0.1165	0.2097	0.1302	0.2343
0.2778	0.5001	0.1213	0.2184	0.1705	0.3069
0.2934	0.5281	0.1288	0.2319	0.1911	0.344
0.3029	0.5452	0.1292	0.2326	0.2374	0.4272
0.307	0.5526	0.1325	0.2385	0.262	0.4716
0.3101	0.5582	0.139	0.2503	0.2624	0.4723
0.3123	0.5622	0.1406	0.253	0.271	0.4878
0.3285	0.5913	0.1478	0.2661	0.3154	0.5676
0.34	0.6121	0.1532	0.2758	0.3296	0.5933
0.3457	0.6222	0.166	0.2989	0.3346	0.6023
0.3706	0.667	0.1736	0.3126	0.349	0.6283
0.3751	0.6753	0.1742	0.3136	0.3569	0.6425
0.3818	0.6872	0.1799	0.3238	0.387	0.6966
0.3819	0.6873	0.1846	0.3323	0.4029	0.7252
0.3932	0.7077	0.1988	0.3578	0.4263	0.7673
0.3939	0.709	0.2067	0.372	0.4593	0.8267
0.3945	0.7101	0.2097	0.3775	0.4633	0.834
0.3986	0.7174	0.2109	0.3796	0.4642	0.8355
0.4084	0.7351	0.2161	0.3891	0.4768	0.8582
0.4297	0.7734	0.2193	0.3948	0.4923	0.8862
0.4376	0.7876	0.2211	0.398	0.5181	0.9326
0.445	0.8011	0.2218	0.3993	0.5271	0.9487
0.4559	0.8207	0.2237	0.4026	0.5344	0.962
0.4616	0.8308	0.2258	0.4064	0.5427	0.9769
0.4629	0.8332	0.235	0.423	0.5636	1.0145
0.4881	0.8786	0.2432	0.4377	0.644	1.1592
0.4978	0.8961	0.2529	0.4552	0.6919	1.2454
0.5035	0.9064	0.2581	0.4646	0.6937	1.2487
0.5059	0.9107	0.2606	0.469	0.7293	1.3128
0.5227	0.9408	0.261	0.4698	0.7458	1.3425
0.5667	1.02	0.3161	0.569	0.7965	1.4338
0.583	1.0494	0.3445	0.6201	0.9062	1.6312
0.5852	1.0534	0.3558	0.6404	0.9265	1.6678
0.5925	1.0665	0.3646	0.6564	0.9573	1.7231
0.6277	1.1298	0.4324	0.7783	1.4003	2.5205

Figure 3 graphically shows the three different sensor models. The graph shows the changes in the currents of sensor is non-linear and made from the noise. Work on the design Sensor array for the detection and classification of the disease is done and have been published in Inderscience journal. Ref. [13]

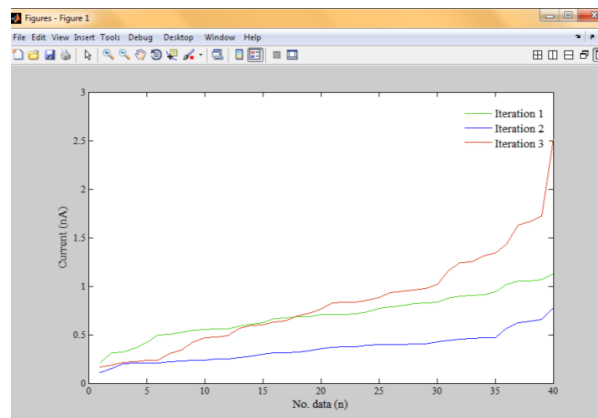


Fig.3. Concentration Vs. sensor currents for three iterations

MATLAB model is based on the results in Table 1. Experimental setup was used to identify the amount equivalent current flowing in a lab Biological sensors drain nanowire sensors by changing the concentration of the analyte is used. During the setup of the experiment, 120 different amount of analyte concentration to detect changes in the drain current regulated. Analyte concentration from 0.06 to 2.5 (nmol/ L) changed and currents corresponding With drain identified and recorded. MATLAB models, to find a table of the values obtained in the laboratory of biological sensors. In order to extend sensor models for all possible input conditions, public input is required to extend the model to sensors. In this work, curve fitting techniques to improve the performance characteristics of the sensor model is adopted.

5. THE CURVE FITTING TECHNIQUES

There are four stages in the fitting curve, which consists of: 1- data transformation , 2- smoothing and filtering, 3- Curve fitting and 4- residual analysis.

5.1. Smoothing and Filtering

Common types of moving average filter is filtering through replacing each data point with the average of the neighboring data points defined within smoothed out. Savitzky-Golay filter that is used in this paper can also be argued as a generalized moving average. Filter coefficients do not weigh a linear least squares the fitting using a polynomial of the known degree, can be deduced. For this reason, a filter, a filter Savitzky-Golay digital smoothing polynomial filters and smoothers, called least squares. Savitzky-Golay than moving average filter can be less successful filter in the absence of a crossing noise. Figure 4 shows an example of currents filter using Savitzky-Golay filter the sensor for long range and $k=3$ and $f = 39$. The results show that the sensor noise is filtered out and therefore improves the performance of the sensor model.

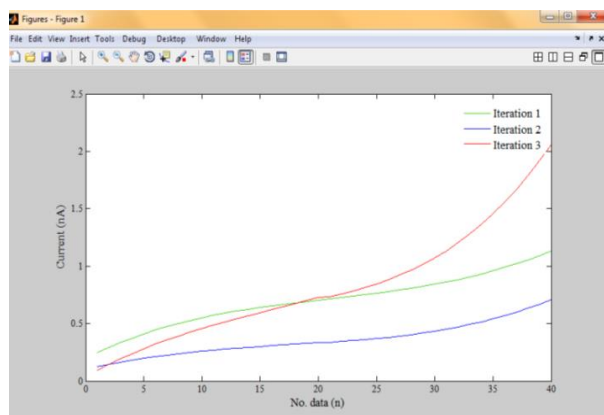


Fig.4. Savitzky-Golay filtering of sensor currents

6. CLASSIFICATION, DIAGNOSIS AND ANALYZE THE CANCER CELLS

Classification and diagnosis can be performed using a variety of techniques that the most prominent among them are the support vector machines, K-nearest neighbor algorithms, neural networks, classification tree and genetic algorithm. In this work, a neural network and K-nearest neighbor algorithm for intelligent drug release system are selected to achieve better results in data classification .Neural network approach to extract the characteristics of the system and the accuracy of K-nearest neighbor algorithm for classification based on test feature is used. In this work, using two different methods to estimate the performance of expert system is done. First test design and analysis and detection of mass spectrometry protein profiles of prostate specific antigen (PSA) using neural networks, and the second experiment design and analysis of cancer detection using principal component analysis and neural network (PCA).

7. DESIGN EXPERT SYSTEM BASED ON ARCHITECTURE OF THE FEEDFORWARD NETWORKS, FFANN

Prostate cancer data to validate expert systems using standard data sets are obtained and stored in a folder. Directory contains two classes of data as the data is control data and cancer. Control data as reference data for training networks for classification of cancerous cells with a desired accuracy is used. During the training phase, the network is trained and weight FFANN network layers have been identified on the basis of net weight obtained in the training phase, data cancer is designed to validate network performance. This network consists of input, hidden layer and output layer. The number of neurons in the hidden layer is 5 and output layer is only one neuron. In men with prostate cancer, PSA level above 4 (ng/ml) will be the current of 0.1407(nmol/l) the stream is about 0.2532 (nA).

The values of model input data into a hidden layer consists of a vector by 2 array is an array is cell concentration in nanomoles per liter and the second array, current corresponding sensor in front of the concentration. Hidden layer weight matrix for the 120 input is a matrix vector by 1×2 array includes 120 vector with dimensions of 2×5 . The output layer contains one neuron weight with 120 matrix size is 5×1 . Input based on noncancerous cells have been classified as the output "1" if the cancer and "0" if the non-cancer. Adopt Levenberg-Marquardt back propagation networks in which the weight is initialized to a random number.

The number of epoch to 1000 period, a period of 120 input vector patterns set .The performance goal is setting 0.401. This number determines the total amount

of time, number of repetitions, and error number needed to reach the target. Network converged in 29 epoch and performance $13^{-10} \times 6.58$, which is much less than the target set for network simulation and thus it is prove the network speed FFANN designed and compared with simulations performed by Eswaran Ushaa Ref. [14] that in the moment of performance is 0.00521, has much less and is close to the desired goal. Also the comparable amount the gradient network trained at the end of training with simulation Ushaa Eswaran has much less and indicates it would fit better and less error rate of the current network.

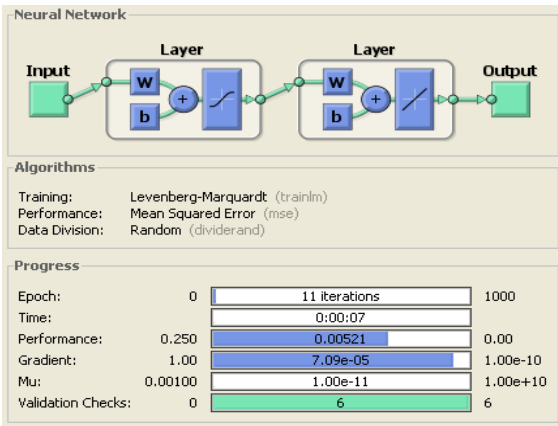


Fig.5. The train MATLAB Model content article Ushaa Eswaran Ref. [14]

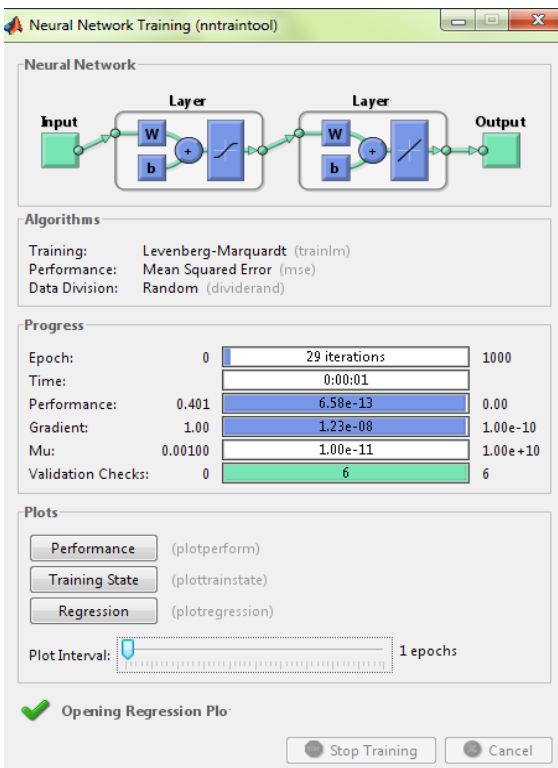


Fig.6. The form of design FFANN Network

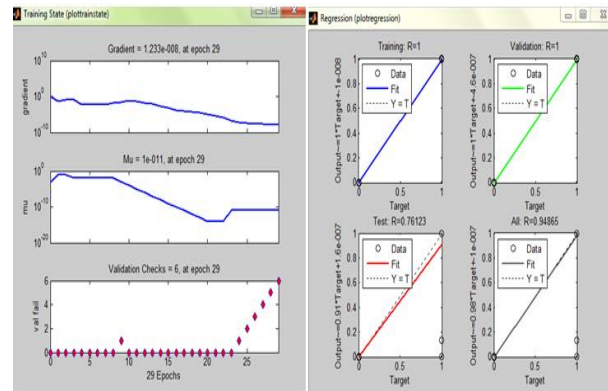


Fig.7. The Curves Fitting And The Results Of Training FFANN Network

As can be seen in Figure 7, the results of the fit function networks trained with graphical charts to preliminary data from the results of experiments in the laboratory with natural Nano-Biosensors obtained is very close to reality is; that this network resulting of carefully trained, and proper select training of the neural network algorithm. After network training, test parameters used to the test to validate network performance.

When the trained network Reaches to reproduce the target , Samples from 20 people randomly data set other than the original data training selected and used to test for cancer. Table 2 is a samples test of network is consistent with the results in Figure 8 Network response to cancer cells in the test with 100% correct and accurate results.

Error! Reference source not found.. The sample Amounts for testing FFANN network after training

Concentration In (nmol/L)	Sensor current Equivalents(nA)	Concentration in (nmol/L)	Sensor current Equivalents(nA)
0.061	0.1099	0.126	0.2269
0.150	0.2698	0.430	0.7742
0.100	0.1814	0.129	0.2322
0.240	0.4324	0.480	0.8642
0.113	0.2033	0.134	0.241
0.280	0.3374	0.550	0.9904
0.115	0.2069	0.138	0.2484
0.343	0.6176	0.590	1.0635
0.120	0.2159	0.1405	0.2528
0.380	0.6836	0.680	1.2233

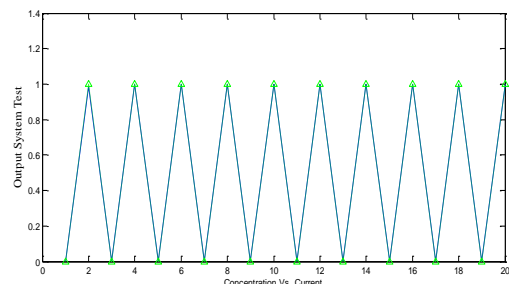


Fig.8. The response of network to test samples

Error! Reference source not found. shows the response of the prototypes system for training the network is obtained according to the diagram, a prototypes network training with only one error in 120 samples or about 99.16% accuracy and responsiveness, this error is only 0.84% that it Results the accuracy response accuracy in comparison with the other simulated network to network.

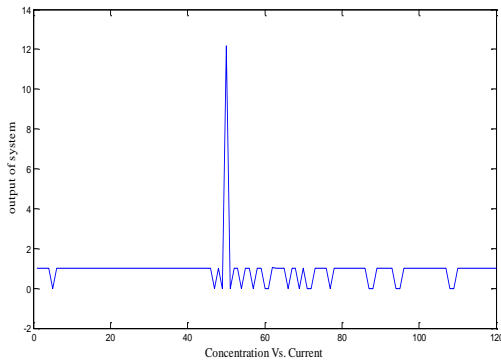


Fig.9. The response network to the training initial sample

The output of a system is "1" or "0" that connected to the pump driver control unit to control the release of drugs to stimulate the release of the drug and monitoring the drug. Network trained to correctly classify the cancer cells and normal cells to take to work. Based on the weight and bias values obtained after successful training network for its performance, with a new set of input data is tested. The classification algorithm using neural networks for classification of cancer and non-cancer cells used. Figure 9 and Figure 10 shows the graphs training and some of the weight matrix and bias layer simulation.

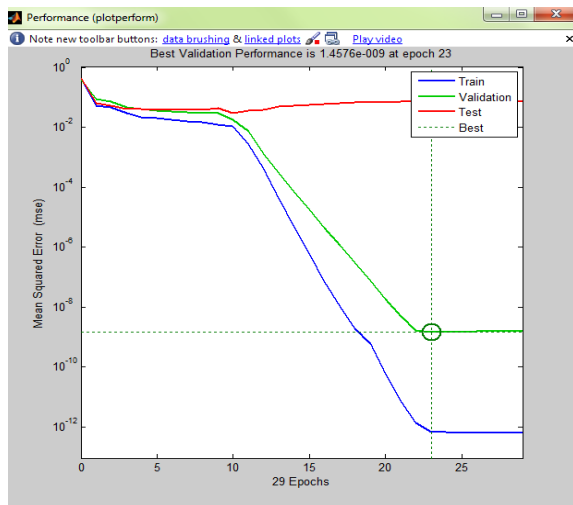


Fig.9. FFANN network training diagram

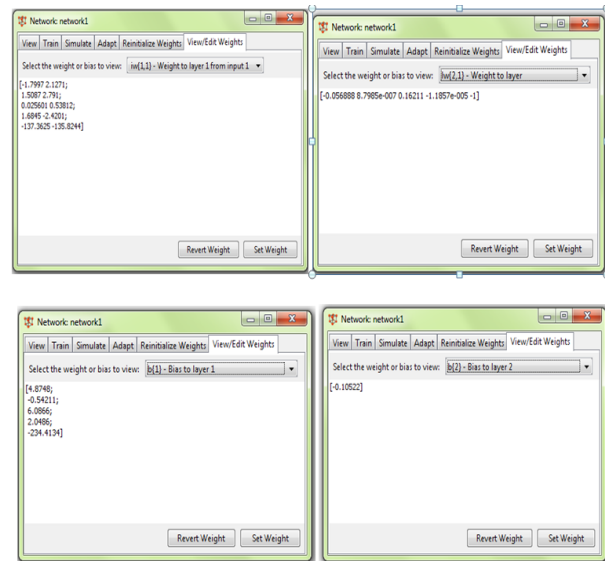


Fig.10. The weight and bias matrices obtained from training of FFANN network

8. CONCLUSION

Diagnosis and drug delivery device set that can automatically detect and monitor cancer, in this work, Designing, modeling and implementation. In this paper, a mathematical model were analyzed for nanowire sensors and changes in the sensor properties with geometric parameters, that this experimental setup can Lead to simulate the development of three of nano-sensors (ISFETs , nanowire and nanoparticles). Nanowire sensor simulation and its response to changes in the concentration of the analyte to be determined. The results show that the developed mathematical model against model real biological sensors, on average and several different data test from cancerous and non-cancerous samples network performance whit correctly identify by 99.28% and network error on the maximum average is only 0.72% that this shows the high accuracy of this network in the other simulations of past. In this analysis there is the bio-sensor model and MATLAB software model ,that Lowered this error in this case development due to accurate results using the bio-sensors for a large number of analyte concentration.

REFERENCES

- [1] M. Beckett,.; cazares, I.; A. vlahou; P. schellhammer,; wright, g.(1995) **“Prostate-specific membrane antigen levels in sera from healthy men and patients with benign prostate hyperplasia or prostate cancer”**.,*Clin. Cancer res.* 1995, 5, 4034-4040.
- [2] N. Dandachi;O. dietze,; C. hauser-kronberger, (2002) Chromogenic in situ hybridization: **“a novel approach to a practical and sensitive method for the detection of her2 oncogene in archival human breast carcinoma”**.,*Lab. Invest.* 2002, 82, 1007–1014.
- [3] C. Henderson,; A. patek, (1998) **“The relationship between prognostic and predictive factors in the**

- management of breast cancer". Breast cancer res. Treat. 1998, 52, 261-288.
- [4] J. Ludwig; J. weinstein. (2005) **"Biomarkers in cancer staging, prognosis and treatment selection"**. Nature rev. Cancer, 5, 845-856.
- [5] J. Landman; Y. chang; E. kavaler; M. droller; B. liu.(1998) **"Sensitivity and specificity of nmp-22, telomerase, and bta in the detection of human bladder cancer"**. Urology 1998, 52, 398-402.
- [6] R. Molina;J. auge; J. escudero; R. marrades ; N.vinolas; E. carcereny; J. ramirez; X. filella. Mucins ca(2008) 125, ca 19.9, ca 15.3 and tag-72.3 as **"tumor markers in patients with lung cancer"**: comparison with cyfra 21-1, cea, scc and nse. Tumor biol. 2008, 29, 371-380.
- T.W. Prow,W.A. rose ,N. wang ,L.M. reece, , Y. Ivov, J.F. leary, (2005). **"biosensor-controlled gene therapy/drug delivery with nanoparticles for nanomedicine"**. proc. Of spie 5692: 199 –208, 2005.
- [7] J.N. Prowsmith,R. grebeJ.H. salazar.,N. wang, N. kotov, G. luty, ,J.F. leary, (2006) **"construction, gene delivery, and expression of dna tethered nanoparticles"**. molecular vision. 12: 606-615, 2006.
- [8] T.W. Prow,R. grebe,C. merges, ,J.N. smith, D.S. mcleod, , J.F. leary,A. gerard ,G.A. Luty,.(2006) **"novel therapeutic gene regulation by genetic biosensor tethered to magnetic nanoparticles for the detection and treatment of retinopathy of prematurity"**. molecular vision 12: 616-625, 2006.6.
- [9] Ushaa eswaran, m.madhavilatha, , (2009) **"disease detection using pattern recognition techniques" national conference on 'emerging trends in information communication technology"**. (etict-08) held in gitam university, india during 19th & 20th december and is published in gitam journal of information communication technology of vol-2 jan - july 2009 number - 1 (issn 0974-4622) pp 34-37.
- [10] Ushaa eswaran, madhusudhana rao, m.s.thakur (2004) **"microprocessor based biosensors for determination of toxins and pathogens in restricted areas of human intervention"**. ic ai'04 ieee sponsored international conference on artificial intelligence held in las vegas, nevada, usa during 21 – 24 june2004.
- [11] Ushaa. S.M.; madhavilatha.m; madhusudhana rao ganji.(2010) - **"development and validation of matlab models for nanowire sensors for disease detection"** .i-manager's journal on future engineering & technology, vol. 6 1 no. 1.2 .
- [12] Ushaa. S.M.; Madhavilatha.M; Madhusudhana Rao Ganji (2011). **"Design and Analysis of Nanowire Sensor Array for Prostate Cancer Detection"**. (Submission code: IJNBM-20274) for the International Journal of Nano and Biomaterials (IJNBM). Int. J. Nano and Biomaterials, Vol. 3, No. 3.
- [13] Ushaa Eswaran, Vivek Eswaran (2012). **"Neural Network Architecture based Software Reference Model for Automated Disease Classification and Detection"**. UNIASCIT, Vol 2 (1), , 183-192.
- [14] Ushaa Eswaran, Vivek Eswaran (2012) **" Neural Network Architecture based Software Reference Model for Automated Disease Classification and Detection "** UNIASCIT, Vol 2 (1), , 183-192.