

Review

Analysis of E. Coli Environment Related to the stages of Cancer

Guangyue Shi¹, T.K. Basak^{2*}, T. Ramanujam³, Madhubala Bhatt³, Deepali Garg³, Richa Garg³,
Sudheer Patil³, Narendra Murtare³, S. Jeybalan³

¹Department of Medicine Oncology, Harbin Medical University, Harbin, China.

^{2*}Krishna Engineering College, Ghaziabad, UP, India.
Krishna Engineering College, Ghaziabad, UP, India.

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Protein kinase C plays an important role in angiogenesis and apoptosis in cancer. During the phase of angiogenesis the growth factor is up regulated where as during apoptosis the growth factor is down regulated. For down regulation of growth factor the pH environment of intra-cellular fluid has a specific range in the alkaline medium. Protein kinase C along with E-coli through interaction of Selenometabolite is able to maintain that alkaline environment for the apoptosis of the cancer cell with inhibition of the growth factor related to antioxidant/oxidant ratio. The present paper through implementation of Artificial Neural Network, also DTREG, has focused on metastasis linked with Capacitance Relaxation phenomena and down regulation of growth factor (VGEF). In this paper a distributed neural network has been applied to a data mining problem for classification of cancer stages in order to have proper diagnosis of patient with PKC sensor simulated in E.coli environment. The Network was trained off line using 270 patterns each of 6 inputs. Using the weight obtained during training, fresh patterns were tested for accuracy in diagnosis linked with the stages of cancer. It is to be noted that simulated E-coli environment of this paper has great impact for the treatment of cancer with monoclonal antibody.

Keywords: Growth factor inhibition, Electrostrictive energy, Capacitance relaxation phenomenon, Antioxidant/Oxidant ratio, ANN, Antibody

INTRODUCTION

It is to be noted that the environment of survival of E. coli over a wide range has been analyzed in relation to proliferation and inhibition of metastasis with cyclic genetic reform mediated through oxidant/antioxidant. The Oxidant/Antioxidant can be simulated in the E-coli environment through the Electrostrictive energy derived from capacitance relaxation shown in figure 1.

Figure 2 and 3 shows the status of electrostrictive energy and capacitance relaxation in cancer cells respectively. It is to be noted that with higher value of electrostrictive energy apoptosis in cancer cell is initiated.

It is interesting to note that the metastasis of the cancer cell can be correlated to capacitance relaxation

phenomenon against pH which is nothing but the E.coli environment and this phenomenon is represented in figure 4.

E. coli related archaeobacteria in lipid peroxidation is influenced by the asymmetry of the lipid and the more the lipid peroxidation less is the relaxation time

Asymmetry is linked with pH gradient mediated by lipid peroxidation. Relaxation of polar head is related to archaeobacteria. Na⁺/H⁺ antiporters cause enhancement of lipid peroxidation. Antiporters maintain alkaline environment where as lipid peroxidation is initiated by antiporters maintaining acidic pH homeostasis of the fluid of the E. coli archaeobacteria. Antiporters initiate lipid peroxidation which sustains pH gradient in the environment of archaeobacteria. Thus the asymmetry of polar head of archaeobacteria (E. coli) is sustained in its pH environment mediated by the antiporters linked with

*Corresponding author email: tkb20042001@yahoo.co.in

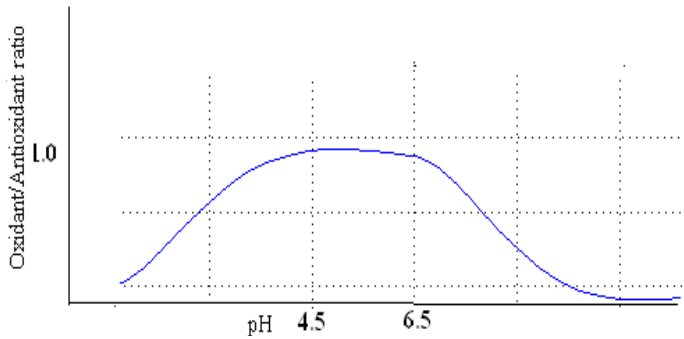


Figure 1. Oxidant/antioxidant ratio of E. Coli w.r.t. pH of its Environment

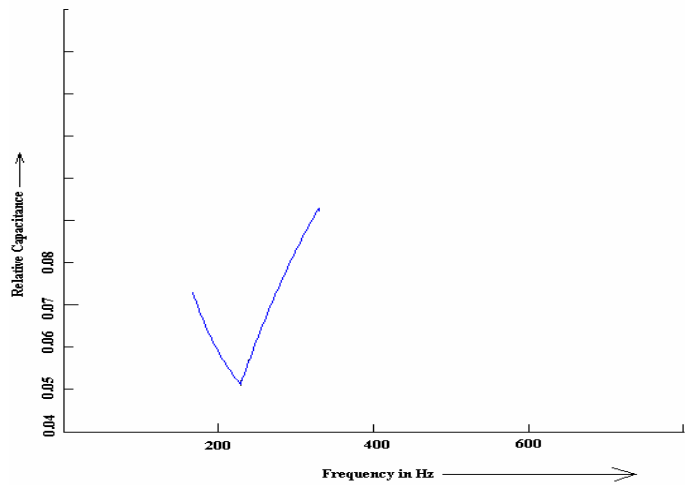


Figure 3. Capacitance relaxation in cancer cells

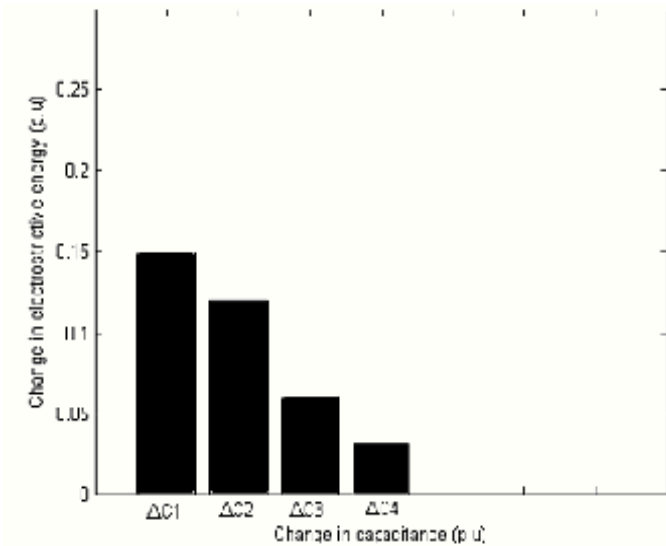


Figure 2. Status of Electrostrictive energy in cancer cells.

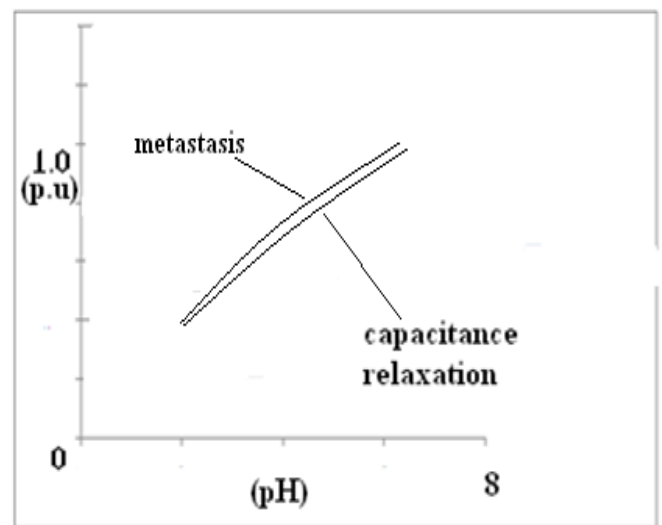


Figure 4. Capacitance relaxation- metastasis curve related to pH

the electrochemical gradient across its membrane. DNA-binding proteins from starved cells (Dps proteins) protect archaeobacteria primarily from oxidative damage. The Oxidative stress influenced by catecholamine [Tapas et al. 2005] causes damage of DNA up to pH from 3 to 4.5 and the effect of antioxidant reduces the oxidative stress beyond pH 4.5. This particular phenomenon has been correlated with the pH for the status of oxidant to antioxidant ratio in cancer cell. Oxidant/antioxidant ratio in E.Coli with lower pH is linked to metastasis and capacitance relaxation phenomenon [Basak et al. 2009; Guanyue et al. 2010]. Debye dispers Tumors induce blood vessel growth (angiogenesis) through Vascular Endothelial Growth Factor (VEGF). Over-expression of VEGF causes increased permeability in blood vessels in simulating angiogenesis. Malignant cells exhibit capacitance Relaxation phenomena and it has been correlated with VEGF. In the process of pH homeostasis

influenced by Ca and NO the cell signaling pathway is modulated by NRF2 that tends to reduce the oxidative stress due to VEGF [Dinel et al. 2005]. This is achieved through VEGF mRNA levels mediated through the increase in expression of intracellular GSH.

Associated oxidative stress causes DNA damage with increase oxidant/antioxidant ratio in E.Coli for pH range 3-4.5. As DNA damage is correlated with increased oxidant/antioxidant ratio in E. coli for tumor progression. Similarly DNA recovery is correlated to decreased oxidant/antioxidant ratio in E. coli when the effect of antioxidant reduces the oxidative stress beyond pH 4.5.

Oxidant/antioxidant balance is an important factor related to initiation and progression of cancer. Clinical

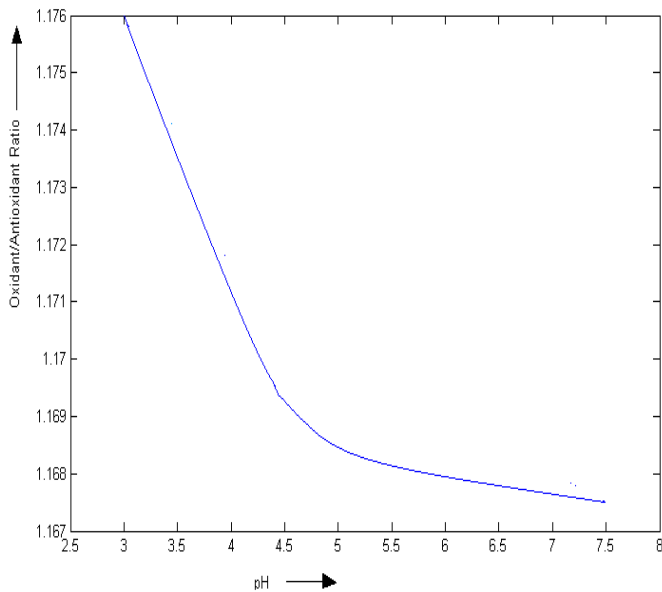


Figure 5a. Oxidant/ antioxidant ratio Vs Ph

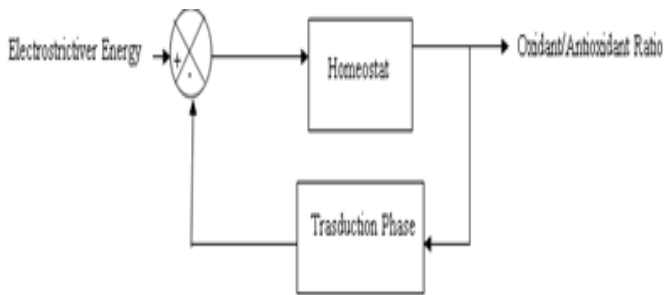


Figure 5b. Generalised model of metastasis/apoptosis

research shows that more the oxidant/antioxidant ratio more is the metastasis. It has been investigated that antioxidant activity occurs at higher values of pH. Referring to Figure 3, we can say that as pH becomes more basic (increasing pH), less will be the oxidant/antioxidant ratio. It can be noted that the environment of survival of *E. coli* over a wide pH range has been analyzed in relation to proliferation and inhibition of metastasis with cyclic genetic reform. Figure 5a. Oxidative stress causes damage of DNA up to pH from 3 to 4.5 and the effect of antioxidant reduces the oxidative stress beyond pH 4.5. This particular phenomenon has been correlated with the pH for the status of oxidant to antioxidant ratio in cancer cell. Oxidant/antioxidant ratio in *E. coli* with lower pH is linked to metastasis (Himmertoglu et al. 2009; Marika et al., 2009; Basak et al. 2009; Tapas et al. 2008). When electrostrictive energy decreases, ratio of oxidant/antioxidant increases [Basak et al. 2008]. Lipid peroxidation relaxation time of lipid of *E. coli* also

increases and pH decreases leading to metastasis. From Figure 4, it is clear that ratio of oxidant/antioxidant decreases with increment of pH. Thus we can conclude that oxidant/antioxidant ratio increases with decrease in pH value. With low acidic pH (pH=3.5), the relaxation time increases which initiates metastasis. Again metastasis can be retrorted with the increase of pH (pH=7.5) with higher value of electrostrictive energy and it causes decrement of oxidant/antioxidant ratio associated with decreased relaxation time. With more metastasis oxidant/antioxidant ratio will increase. With lower metastastasis oxidant/antioxidant ratio will decrease.

Modeling and Simulation

Figure 5b shows a generalized model of metastasis and Apoptosis in cancer. As we are interested in the status of oxidant/antioxidant ratio with respect electrostrictive energy [Basak et al. 2009; Shivamurthy et al. 2008], the input to the model is electrostrictive energy [Tapas et al. 2005; Guangyue et al. 2010; Basak 2007] and output of the model is oxidant/antioxidant ratio. The homeostat and transduction phase are linked with lipid per oxidation mediated by antiporters in *E. coli* archaeobacteria. The incremental input electrostrictive energy is applied to the model on the basis of pH homeostasis linked with capacitance relaxation phenomenon.

Implementation of Model Using Ann

Description of experiments

Experimental set up

Data such as pH, capacitance relaxation, metastasis, oxidant-antioxidant ratio have been collected for 1000 patients. A total of 6 parameters about cancer have been collected from cancer patients linked with capacitance relaxation [Guangyue et al. 2010; Dinel et al. 2005]. The input parameters are pH, metastasis, oxidant and antioxidant ratio, capacitance relaxation value and estrogen receptors ratio and the output parameter is the final stage in which the patient belongs.

In Figure 6, we can see how the misclassification percentage varies on varying no. of neurons in hidden layer. The optimum design shows there should be 13 neurons in hidden layer for minimum classification and accurate results.

Figure 7 shows misclassification tables for training and validation. The average misclassification of validation data comes out to be around 11.5%.

The graph below is a plot showing number of neurons in hidden layer Vs percent misclassification. For 13 neurons in hidden layer, error comes out to be minimum.

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===== Model Size Summary Report =====

Network size evaluation was performed using a 20% hold-back sample.

Hidden layer 1 neurons  % Misclassifications
-----
      2                15.38462
      3                15.38462
      4                15.38462
      5                15.38462
      6                11.53846
      7                11.53846
      8                15.38462
      9                15.38462
     10                15.38462
     11                15.38462
     12                15.38462
     13                7.69231 <-- Optimal size
     14                15.38462
     15                15.38462
     16                23.07692
     17                15.38462
     18                30.76923
     19                15.38462
     20                19.23077

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The network will be built using 13 neurons for hidden layer 1.

Figure 6. Table displaying Model size

Ann as a Classifier in Matlab

No. of samples used for training=260
 Same samples when used for validation that gives error =18

Therefore, misclassification= $\frac{18}{260} * 100 = 6.9 \%$

No. of iterations taken is upto 2000
 No. of neurons in hidden layer is taken=5
 Tolerance=0.01
 Momentum is taken=1.2 and Learning Rate is taken=0.8
 Sumerror initially is taken=0
 No. of iterations starting from 0 will go upto 2000 till sumerror is greater than tolerance.

The above graph is a plot how sumerror varies with increasing no. of iterations. The no. of iterations in our proposed model is around 2000 for desired sumerror and tolerance. Figure 8 and 9

Below given are the snapshots of how the sumerror decreases with the increase in no. of iterations. Iterations upto which process will continue is 2000, so it is shown in snapshot that on completion of 2000 iterations, we get the final weight matrices.

RESULTS OF ANN IMPLEMENTATION IN MATLAB

Table 1 given below shows the resultant weight matrix for input and hidden layer.

DISCUSSION AND CONCLUSION

In the present paper partial dataset are prepared with the relevance angiogenesis in cancer linked with capacitance relaxation phenomena and metastasis in the pH environment of E-coli with Protein Kinase C. This data is

===== Misclassification Tables =====

--- Training Data ---

Category	-----Actual-----		-----Misclassified-----			
	Count	Weight	Count	Weight	Percent	Cost
1	8	8	8	8	100.000	1.000
2	52	52	2	2	3.846	0.038
3	43	43	0	0	0.000	0.000
4	27	27	6	6	22.222	0.222
Total	130	130	16	16	12.308	0.123

--- Validation Data ---

Category	-----Actual-----		-----Misclassified-----			
	Count	Weight	Count	Weight	Percent	Cost
1	8	8	8	8	100.000	1.000
2	52	52	4	4	7.692	0.077
3	43	43	0	0	0.000	0.000
4	27	27	3	3	11.111	0.111
Total	130	130	15	15	11.538	0.115

Figure 7. Tables showing Misclassification

mind separately using decision based data mining algorithm. The same data set are used for classification in ANN with Back propagation algorithm. The classifier is used for prediction of the status of the subject with cancer in different stages of metastasis corresponding to respective pH range of the intra-cellular fluid stimulated in E-coli environment with Protein Kinase C. This

prediction in respect of the subject related to the stages of cancer may be useful for the Healthcare Management and treatment of cancer patient.

In ANN implementation learning rate with a variable function also the error involving the stages in metastasis is 6% to 8% linked with the stimulated environment of E-coli corresponding to the pH of intra-cellular fluid. It is to

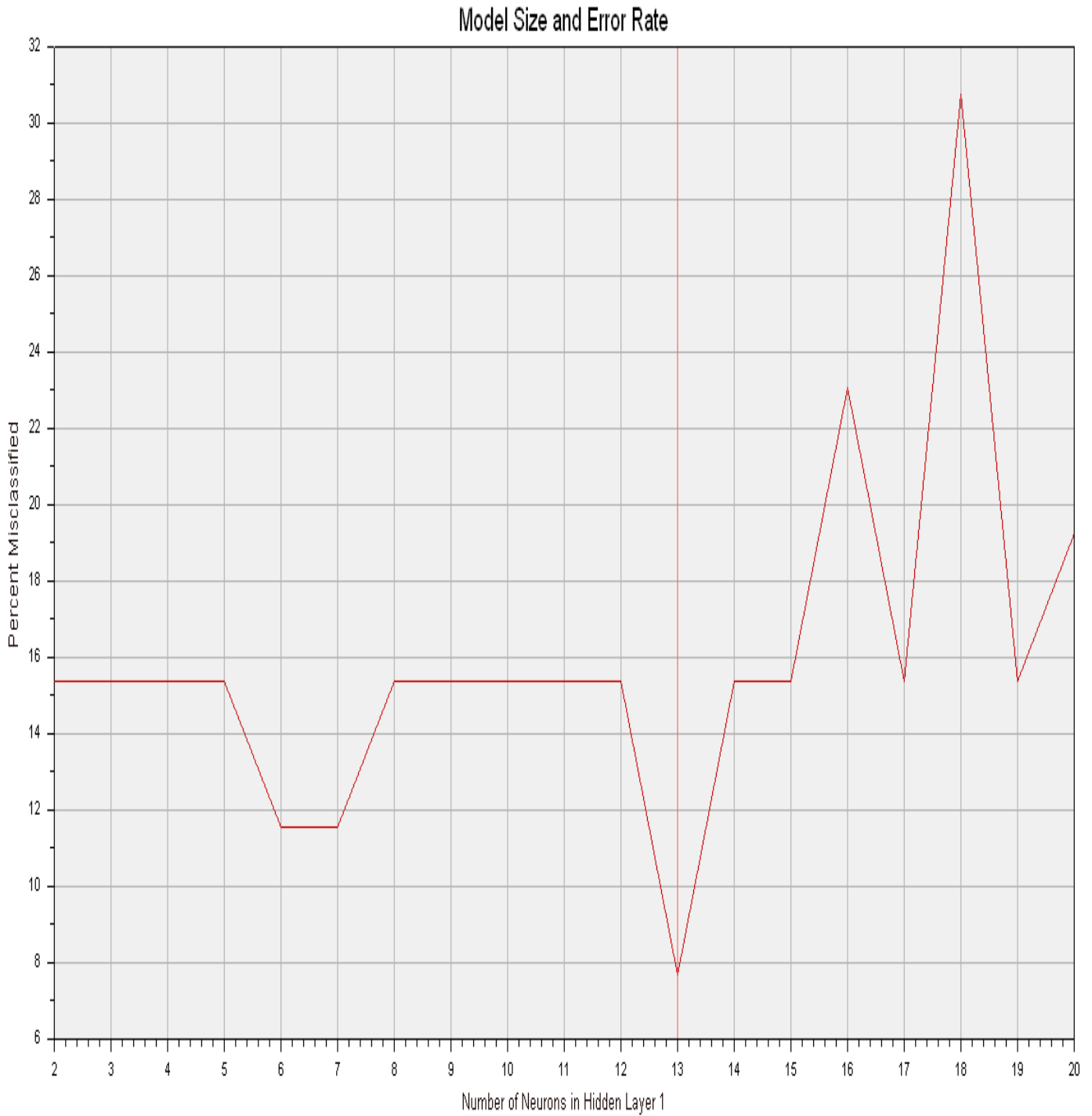


Figure 8. Graph of Model Size Vs Error Rate

be noted that simulated E-coli environment of this paper has great impact for the treatment of cancer with monoclonal antibody.

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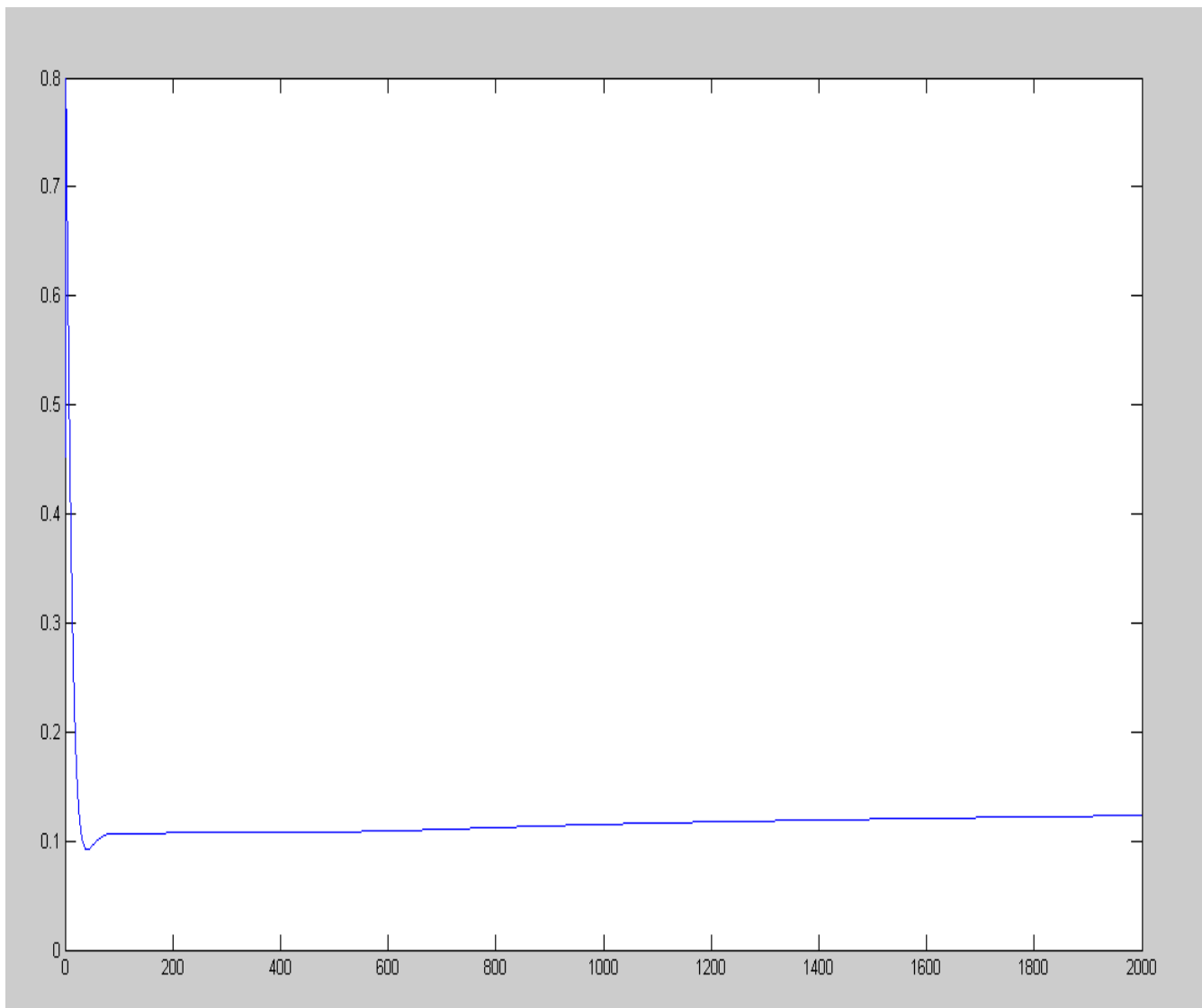


Figure4.5: Graph of sumerror Vs iterations

Table 1 : Weight Matrix

Wih					Whj
-1.8247	1.085	-6.6023	-	-2.4974	-0.34443
-4.3012	-3.9735	7.6455	0.42835	0.52438	0.47733
-	0.26892	-1.7553	-	1.5206	1.4617
0.74473	-	-1.4084	0.15328	-4.2045	-5.1274
0.41868	0.70051	-	-3.5615	-3.8915	1.9881
-3.2854	-1.0747	0.36513	0.74208	0.12508	0.070157
1.3873	0.38019	-1.5126	2.3367		

Wih→weight between input layer neuron and hidden layer neuron
 Whj→weight between hidden layer neuron and output layer neuron

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