ISTANBUL UNIVERSITY –
JOURNAL OF ELECTRICAL & ELECTRONICS ENGINEERING

YEAR : 2007 (443 – 458)
VOLUME : 7
NUMBER : 2

MODELING ELF ELECTROMAGNETIC FIELD EFFECTS ON SKIN'S HYDROXYPROLINE LEVEL USING NEURAL NETWORKS

Ayşe G. CANSEVEN[1] ***Gülay TOHUMOGLU[2]**
Abdükadir ÇEVİK[3] **Nesrin SEYHAN[4]**

[1, 4]Department of Biophysics, Faculty of Medicine, Gazi University, 06510 Ankara, TURKEY
[2]Electrical and Electronics Engineering, University of Gaziantep, 27310 Gaziantep, TURKEY
[3] Civil Engineering, University of Gaziantep, 27310 Gaziantep, TURKEY

[1]E-mail : canseven@gazi.edu.tr [2]E-mail : g_tohumoglu@gantep.edu.tr
[3]E-mail : akcevik@gantep.edu.tr [4]E-mail : seyhan@gazi.edu.tr

ABSTRACT

Skin serves as a first target of the external fields, since its connective tissue content is high which reflects the biochemical and physiological conditions of the skin and has a positively charged collagen molecule. This study has two main purposes: firstly, it was planned to assess whether the skin of guinea pigs was affected by magnetic fields (B) by determining the collagen synthesis in the skin exposed to 50 Hz magnetic fields of 1 mT, 2 mT and 3 mT with the periods of 4 hours/day and 8 hours/day for 5 days and secondly, it was aimed to model this effect on hydroxyproline concentrations in the skin using Neural Networks. One of the important tasks regarding these types of studies is the modeling of the effect for further use without waste of animal which will form as a database for researchers. In this sense, Neural Networks have been used to serve as a robust tool for the modeling of complex relationships that exists between dependent and independent variables where this relationship can not be effectively modeled by conventional regression methods. A novel approach for the selection of optimal Neural Network architecture has been used. The accuracy of the proposed NN model is defined by standard deviation and correlation coefficient which is found to be quite high (R=0.98). Thus parametric studies are performed to see the influence of each parameter by using the proposed NN model. The results of the study are very promising as it will serve as a data base for researchers in these kinds of studies.

Keywords: *Neural Networks, skin, collagen synthesis, hydroxyproline, ELF magnetic field.*

1. INTRODUCTION

ELF EMFs is a form of non-ionizing EMF radiation which has low energy. This energy can influence physiological processes in organisms under certain conditions [1-4]. Although therapeutic potentials of ELF EMF have been extensively used in non-union bone fracture healing and wound healing [5-16], the number of investigations on the biological effect of EMFs has increased as to whether or not they are harmful to humans. Possible associations between exposure to EMFs and serious health problems have been reported by epidemiological and laboratory researches over the past two

Received Date:26.10.2006
Accepted Date: 05.12.2007

decades [14-28]. As a major health effect, these 50 Hz / 60 Hz EM fields may modulate the occurrence of cancer [29-33]. US National Academy of Sciences in 1996 suggested that residence near power lines was associated with an elevated risk of childhood leukaemia (relative risk RR=1.5), but not with other cancers [32]. ELF of magnetic fields was classified as a "possible human carcinogen" by The International Agency for Research on Cancer-IARC [33]. Considerable evidence has accumulated demonstrating that nonthermal exposures of cells and tissue systems and experiment animals to extremely low frequency (ELF) electromagnetic fields (< 300 Hz) can elicit changes on synthesis of DNA, RNA and collagen, free radical processes, natural antioxidant systems, respiratory burst system, immune system activities and electrolytes, tissue division and tissue surface properties [18,19, 24-29, 34-36].

Skin possesses endogenous electrical properties [11]. The various layers of the skin also differ with regard to their electrical properties.The two main measurements used have been the surface potential measurements and the electrical resistance of the skin. Human skin potentials from the stratum corneum with respect to dermis have been recorded as -23±9 mV by Barker and Foulds [37]. The base levels of the skin resistance vary from 10 KΩ.cm^2 (kilo ohm.cm^2) to 500 kΩ. cm^2, for damp and very dry and scaly skin, respectively. Connective tissue reflects the biochemical and physiological conditions of the skin and has a positively charged collagen molecule [12-14, 16]. Hydroxyproline makes approximately 9-13% of the collagen [38]. Thus, biochemical and physiological reactions in the skin have been affected via externally applied electricity [14,16,39].

This study was planned to assess whether the skin of guinea pigs was affected by magnetic fields (B) by determining the collagen synthesis in the skin exposed to 50 Hz magnetic fields of 1 mT, 2 mT and 3 mT with the periods of 4 hours/day and 8 hours/day for 5 days and to model this effect on hydroxyproline concentrations in the skin using Neural Networks based on experimental results. One of the important tasks regarding these types of studies is the modeling of the effect for further use without waste of animal which will form as a database for researchers. In this sense, Neural Networks (NNs) have been used to serve as a robust tool for the modeling of complex relationships that exists between dependent and independent variables where this relationship can not be effectively modeled by conventional regression methods. There are various studies in literature on the NN modeling Electric field effect on tissues and enzymes [40-42]. However NNs have not been used as a tool for the modeling of ELF magnetic field's effect on hydroxyproline concentrations in the skin so far which is the main scope of this study. In this applications, also parametric studies are performed to see the influence of each parameter by using the proposed (optimal) NN model.

The paper is organized as follows: In the following section, Experimental studies will be given. In Section 3, a brief overview of Neural networks and the selection of optimal neural network process have been presented. Neural network modeling is applied to experimental data in Section 4. In the last section, the conclusions are expressed.

2. EXPERIMENTAL STUDIES

Sixty three 10-12 weeks old (weighing 250-300 g) male guinea pigs were used. The experimental protocol was reviewed and approved by the Laboratory Animal Care Committee of Gazi University (Report no: 36-7838).

Magnetic fields were generated by a specially designed pair of Helmholtz coils. The exposure system was built by us as previously desribed in detail [43]. Fifty four guinea gips were divided into six groups and exposed to 50 Hz magnetic fields of 1 mT, 2 mT and 3 mT for the periods of 4 hours/day and 8 hours/day for 5 days. Nine animals served as controls, and were maintained under the same conditions as the other animals without being exposed to any magnetic fields. At the end of the exposure times, skin hydroxyproline concentrations of exposed and unexposed guinea pigs were determined by Woessner's modified method [12-14, 16, 44]. Mann - Whitney U test was applied for statistical analysis to see the differences between exposed groups and controls. As indicated in this paper, the term "skin" refers to epidermis and to the papillary and reticular layers of dermis, excluding the panniculus adiposus and panniculus carnosus. Hairs were carefully

removed with electric clippers before taking the specimens.
Skin's hyroxyproline contents obtained from magnetic fields (B) exposed and unexposed animals have been evaluated to model the effect of 50 Hz magnetic fields (B) of 1 mT, 2 mT and 3 mT by using the optimal NN based on experimental results.

3. A BRIEF OVERVIEW OF NEURAL NETWORKS

A Neural Network is a 'machine' that is designed to model the way in which the brain performs a particular task or function of interest, the network is usually implemented using electronic components or simulated in software on a digital computer. Neural networks are an information processing technique built on processing elements, called *neurons* that are connected to each other [45].

The main component of this model is the structure of its information processing unit. A biological neuron is made up of four main parts: dendrites, synapses, axon and the cell body. The dendrites receive signals from other neurons. The axon of a single neuron serves to form synaptic connections with other neurons. The cell body of a neuron sums the incoming signals from dendrites. If input signals are sufficient to stimulate the neuron to its threshold level, the neuron sends an impulse to its axon. Artificial neuron shown in Fig. 1 is the basic element of a neural network which consists of three main components namely as weights, bias ,and an activation function

Figure 1 Basic Elements of an Artificial Neuron

where

$$u_i = \sum_{j=1}^{H} w_{ij} x_j + b_i \qquad (1)$$

The summation u_i is transformed as the output using a scalar-to-scalar function called an "activation or transfer function" as follows:

$$O = f(u_i) \qquad (2)$$

Activation functions serve to introduce nonlinearity into neural networks which makes NNs so powerful.

Neural networks are commonly classified by their network topology, (i.e. feedback , feedforward) and learning or training algorithms (i.e. Supervised , Unsupervised). For example a multilayer feedforward neural network with backpropagation indicates the architecture and learning algorithm of the neural network.

Back propagation algorithm shown in Figure 2 is used in this study which is the most widely used supervised training method for training multilayer neural Networks due to its simplicity and applicability. It is based on the generalized delta rule and was popularized by Rumelhart et.all [46]. As it is a supervised learning algorithm, there is a pair of input and corresponding output.The algorithm is simply based on a weight correction procedure. It consists of two passes: a forward pass and a backward pass. In the forward pass, first, the weights of the network are randomly initialized and an output set is obtained for a given input set where weights are kept as fixed. The error between the output of the network and the target value is propagated backward during the backward pass and used to update the weights of the previous layers.

Figure 2. Backpropagation Algorithm

3.1 OPTIMAL NN MODEL SELECTION

The performance of a NN model mainly depends on the network architecture and parameter settings. One of the most difficult tasks in NN studies is to find this optimal Network architecture which is based on determination of numbers of optimal layers and neurons in the hidden layers by trial and error approach. The assignment of initial weights and other related parameters may also influence the performance of the NN in a great extent. However there is no well defined rule or procedure to have optimal network architecture and parameter settings where trial and error method still remains valid. This process is very time consuming.

In this study Matlab NN toolbox is used for NN applications. Various Backpropagation Training Algorithms are used. Matlab NN toolbox randomly assigns the initial weights for each run each time which considerably changes the performance of the trained NN even all parameters and NN architecture are kept constant. This leads to extra difficulties in the selection of optimal Network architecture and parameter settings. To overcome this difficulty a program has been developed in Matlab which handles the trial and error process automatically. The program tries various number of layers and neurons in the hidden layers both for first and second hidden layers for a constant epoch for several times and selects the best NN architecture with the minimum MAPE (Mean Absolute % Error) or RMSE (Root Mean Squared Error) of the testing set, as the training of the testing set is more critical. For instance a NN architecture with 1 hidden layer with 7 nodes is tested 10 times and the best NN is stored where in the second cycle the number of hidden nodes is increased up to 8 and the process is repeated. The best NN for cycle 8 is compared with cycle 7 and the best one is stored as best NN. This process is repeated N times where N denotes the number of hidden nodes for the first hidden layer. This whole process is repeated for changing number of nodes in the second hidden layer. More over this selection process is performed for different backpropagation training algorithms such as trainlm, trainscg and trainbfg. The program begins with simplest NN architecture i.e. NN with 1 hidden node for the first and second hidden layers and ends up with optimal NN architecture. The flowchart of the whole selection process is given in Figure 3. Further information regarding the application of optimal NN model selection process can be found in references [47-49].

Figure 3. The flowchart of the whole selection process

4. APPLICATION OF NEURAL NETWORK

The main purpose of this study is to model the effect of 50 Hz magnetic fields (B) of 1 mT, 2 mT and 3 mT on hydroxyproline concentrations in the skin using Neural Networks based on experimental results.

Guinea pigs were exposed to the B fields of 1 mT, 2 mT and 3 mT, with periods of 4 and 8 hours/day for 5 days in 6 different groups. Skin hydroxyproline content of field exposed groups with respect to controls are given in Table 1. Hydroxyproline concentrations of guinea pigs exposed to the 1 mT field were found decreased with respect to controls. B fields of 2 mT and 3 mT increased the hydroxyproline concentrations of exposed guinea pigs, 2 mT was found to be more effective than 3 mT for the exposure times of 4 hours/day, whereas 3 mT was found more effective than 2 mT for the exposure times of 8 hours/day [14, 16]. These experimental results formed a database to model the effect of 50 Hz magnetic fields (B) of 1 mT, 2 mT and 3 mT on hydroxyproline concentrations in the skin using Neural Networks.

The experimental results are divided into train and test sets where patterns in test set are randomly selected among the experimental database shown in bold characters given in Table 2. The optimal NN architecture was found to be 3-5-1 NN architecture with logistic sigmoid transfer function (logsig). The training algorithm was quasi-Newton backpropagation (BFGS). The prediction of the proposed NN model vs. actual experimental values are given in Table 2. Statistical parameters of normalized values of learning and training sets are presented in Table 3.

Table 2 Results of NN model vs Experimantal results

Table 3 Statistical Parameters for NN Model

The performance of the proposed NN model vs. experimental result is shown in Figure 4.

Figure 4 Performance of NN vs Test Results

It is obvious from statistical results (R=0.98) above that the proposed NN model accurately learned to map the relationship between varying parameters. Thus the trained NN models proposed in this study were used to conduct an extensive parametric study to investigate the effect of changing parameters on hydroxyproline levels. In Figures 5-12, interesting outcomes are observed on the graphs of trends. The trend of parameters with each other shows a parabolic relationship in general. The general trend of hydroxyproline level was found to be decreasing for 1 mT and increasing for 2 mT and 3 mT. From Figure 9, it is seen that the increase in hydroxyproline level for 2 mT is observed to be much more sharper than 3 mT for time duration of 5 hours. The experimental results also show that the increase in hydroxyproline level for 2 mT is observed to be much more sharper than 3 mT for time duration of 4 hours. Therefore it is verified that the trained neural network produceses internal data values of experimental data ranges. On the other hand, as duration increases up to 8 hours, the difference between 2 mT and 3 mT decreases. A detailed parametric study should perhaps be the scope of another article.

Figure 5. Influence of time to hydroxyproline output (Magnetic Field = 1 mT)

Figure 6. 3D Surface plot of Influence of time to hydroxyproline output (Magnetic Field = 1 mT)

Figure 7. Influence of time to hydroxyproline output (Magnetic Field = 3 mT)

Figure 8. 3D Surface plot of Influence of time to hydroxyproline output (Magnetic Field = 3 mT)

Figure 9. Influence of EMF to hydroxyproline output (Time Duration= 4hr)

Figure 10. 3D Surface plot of Influence of EMF to hydroxyproline output (Time Duration= 4hr)

Figure 11. Influence of EMF to hydroxyproline output (Time Duration= 8hr)

Figure 12. 3D Surface plot of Influence of EMF to hydroxyproline output (Time Duration= 8hr)

5. CONCLUSIONS

In this study, hydroxyproline levels in the skin of guinea pigs exposed to 50 Hz magnetic fields of 1 mT, 2 mT and 3 mT were modeled using NNs. The accuracies of the proposed NN models are defined by the standard deviations and correlation coefficients found to be quite high (98%) for the ordered data sets. Thus parametric studies are performed using these NN models to investigate the effect of magnetic field on hydroxyproline levels in the skin for varying parameters i.e. exposure duration. As a result of this study, it can be concluded that NNs can be effectively used to model complex relationships especially where no valid models exist as in the case of hydroxyproline levels in the skin considered in this study. Furthermore the proposed NN enables to determine the possible triggering level(s) through studying a greater number of application periods and field intensities without additional experimental studies in the ongoing parts of our study. Thus it serves as a data base for researchers in these kind of fields.

REFERENCES

[1] Tenford, T.S., "Interaction of ELF Magnetic Fields with Living Matter" in *CRC Handbook of Biological Effects of Electromagnetic Fields* (POLK, C., POSTOW, E., eds.), CRC Press, Boston, 197-228, 1986

[2] Frey, A., *On the Nature of Electromagnetic Field Interactions with Biological Systems*, Austin, USA: Landes Company, Medical Intelligence Unit, R.G. ,1994

[3] Tenforde, T.S., "Biological Responses to Static and Time-Varying Magnetic Fields" in *Electromagnetic Interaction with Biological Systems* (LIN, J.C., ed.), 83-108, Plenum Press, New York, 1989

[4] Polk, C., *Introduction in CRC Handbook of Biological Effects of Electromagnetic Fields* (Polk, C., Postow, E., eds.), 1-27, CRC Press, Boston, 1986

[5] Kanje, M., Rusovan, A., Sısken, B., Lundborg, G., "Pretreatment of Rats with Pulsed Electromagnetic Fields Enhances Regeneration of the Sciatic Nevre", *Bioelectromagnetics*, 14, 353-359, 1993

[6] Frank, C., Schachar, N., Dıttrıch, D., Shrıve, N., Phıll, D., Dehaas, W., Edwards, G., "Electromagnetic Stimulation of Ligament Heling in Rabbits", *Clin. Orth. Rel. Res.*, 175, 263-271, 1983

[7] Leaper, D.J., Foster, M.E., Brennan, S.S., Davıes, P.W., "Experimental Study of the Influence of Magnetic Fields on Tissue Wound Healing", *J. Trauma,* 25, 1083-1084, 1985

[8] Hınsenkamp, M., Tuerlınckx, B., Rooze, M., "Effects of ELF Fields on Bone Growth and Fracture Repair" in *Biological Effects and Dosimetry of Static and ELF Electromagnetic Fields* (GRANDOLFO. M., MICHAELSON, S.M., RINDI, A., eds.), 441-446, Plenum Press, New York, 1985

[9] Garcıa, P.G., De La Cal, A.M., "Enhancement of Bone Healing by an Exogenous Magnetic Field and the Magnetic Vaccine", *J. Biomed. Eng.*, 7, 157-160, 1985

[10] Gupta, T.D., Jaın, V.K., Tandon, P.N., "Comperative Study of Bone Growth by Pulsed Electromagnetic Fields", *Med. Biol. Eng. Comput.*, March, 113-120, 1991

[11] Canseven AG., "Electrical Properties of the Skin." *Gazi Med J* 3: 41- 46, 1992.
[12] Canseven AG, Atalay Seyhan N., "Is It Possible to Trigger the Collagen Synthesis by Electric Current in Skin Wounds?" *Indian J Biochem Biophys* 33: 223-227, 1996.
[13] Canseven AG, Atalay Seyhan N., "Electric Current-Collagen Synthesis Interaction in Wound Healing –I." *Turkish Med J*, *Turkish* , 2 : 71-77, 1995.
[14] Canseven A.G., Seyhan N., "Do 50 Hz Magnetic Fields Affect Skin's Collagen Synthesis?", *Indian Journal of Biochemistry and Biophysics*, Nov. 2006 (accepted).
[15] Güler G, Atalay Seyhan N., "Changes in Hydroxyproline Levels in Electric Field Tissue Interaction." *Indian Journal of Biochemistry and Biophysics* 33 : 531-533, 1996.
[16] Canseven A.G., Seyhan N., "Çevresel ELF Manyetik Alanların Etkileri : Kobay Deri Kollagen Sentezinde Değişimler ve Deney Hayvanından İnsana Ölçülendirme," *Gazi Tıp Dergisi,* 16 (4) : 160 – 165, 2005
[17] Mevıssen, M., Wahnschaffe, U., Löscher, W., Stamm, A., Lerchl, A., "Effects of AC Magnetic Fields on DMBA-Induced Mammary Carcinogenesis in Sprague-Dawley Rats" in *Electricity and Magnetism in Biology and Medicine* (BLANK, M., ed), 413-415, San Francisco Press, Inc., USA (1993)
[18] de Seze, R., Bouthet, C., et al., "Effects of Time-Varying Uniform Magnetic Fields on Natural Killer Cell Activity and Antibody Response in Mice." *Bioelectromagnetics* 14: 405-412, 1993
[19] Garcia-Sancho, J., Montero, M., et al., "Effects of Extremely Low Frequency Electromagnetic Fields on Ion Transport in Several Mammalian Cells." *Bioelectromagnetics* 15 : 579-588, 1994
[20] Graham, C., Cook, M.R., Riffle, D.W., "Human Melatonin During Continuous Magnetic Field Exposure." *Bioelectromagnetics* 18 : 166-171, 1996
[21] Lin, R.S.; Dischinger, P.C.; Conde, J., Farrell, K.P. "Occupational exposure to electromagnetic fields and the occurrence of brain tumors. An analysis of possible associations." *J. Occup Med*. **27:** 413-419; 1985.
[22] Preston-Martin, S.; Mack, W.; Henderson, B.E., "Risk factors for gliomas and meningiomas in males in Los Angeles County," *Cancer Res*. 49: 6137-6143; 1989.
[23] Bastuji-garin, S.; Richardson, S.; Zittoun, R., "Acute leukaemia in workers exposed to electromagnetic fields." *Eur. J. Cancer*. 26: 1119-1120; 1990.
[24] Canseven, A.G., Seyhan, N., Mirshahidi, S., Imir, T., "Suppression of Natural Killer Cell Activity on *Candida Stellatoidea* by a 50 Hz Magnetic Field." *Electromagnetic Biology and Medicine,* 25 (2) : 79-85, 2006
[25] Seyhan N., Canseven A. G. & Güler G., "Animal Studies on the Effects of ELF and Static EMF." In Ayrapetyan S.N., Markov M.S., eds. *Bioelectromagnetics Current Concepts, The Mechanisms of the Biological Effect of Extremely High Power Pulses* . NATO Security through Science Series B: Physics and Biophysics, Vol. 5, pp: 195-212, 2006
[26] Canseven, A.G., Seyhan, N., et al., "Extremely Low Frequency Electromagnetic Field Effect on Brain Tissue and Blood Plasma Electrolytes." *Med & Biol Eng & Comput* 37 (Suppl. 2) : 1336-1337, 1999
[27] Canseven A.G., Seyhan N., Aydın A., Çevik C., Işımer A., "Effects of Ambient ELF Magnetic Fields : Variations in Electrolytes Levels of Brain and Blood Plasma." *Gazi Medical Journal* 16 : 121 – 127, 2005
[28] Yokus, B.; Cakir, D. U.; Akdag, M. Z., Sert, C.; Mete, N., "Oxidative DNA damage in rats exposed to extremely low frequency electromagnetic fields." *Free Radical Res.* 39: 317-323; 2005.
[29] Byus, C.V., Pieper, S.E., Adey, R., "The effects of low-energy 60 Hz environmental electromagnetic fields upon the growth related enzyme ornithine decarboxylase." *Carcinogenesis* 8 : 1385-1389, 1987
[30] Wertheimer, N.; Savitz, D.A.; Leeper, E., "Childhood cancer in relation to indicators of magnetic fields from ground current sources." *Bioelectromagnetics* 16: 86-96;1995.
[31] Hakansson, N.; Floderus, B.; Gustavsson, P.; Johansen, C.; Olsen J.H., "Cancer incidence and magnetic field exposure in industries using resistance welding in welding in Sweden." *Occup. Environ. Med.* 59: 481-486; 2002
[32] WHO Fact Sheet N° 263. Electromagnetic Fields and Public Health - Extremely Low Frequency Fields and Cancer, October 2001.

(http:// www.who.int/docstore/peh-emf/publications/facts_press/efact/efs263.html) .

[33] IARC Monographs On The Evaluation Of Carcinogenic Risks To Human Non-Ionizing Radiation. Part 1 : *Static and Extremely Low Frequency (ELF) Electric and Magnetic Fields.* IARCPress, France, Lyon: Vol. 80, 2002

[34] Lai, H.; Singh, NP., "Magnetic field-induced DNA strand breaks in brain cells of the rat." *Environmental Health Perspectives*. 112: 687-694; 2004.

[35] Singh, L P.; Lai, H., "60- Hz magnetic field exposure induces DNA crosslink in rat brain cells." *Mutat Res.,* 400: 313-320; 1998.

[36] Brocklehurst, B.; Mclauchlan, K.A., "Free radical mechanism for the effects of environmental electromagnetic fields on biological systems." *Int J Radia. Biol.* 69: 3-24; 1996.

[37] Foulds IS, Barker AT., "Human Skin Battery Potentials and Their Possible Role in Wound Healing." *British J. Dermatology* 109: 515-522, 1983.

[38] Bhagavan N.V., *Medical Biochemistry*, Boston : Jones and Bartlett Publishers Inc, 1992.

[39] Ahmadian S., Zarchi S.R, Bolouri B., "Effects of extremely low frequency pulsed electromagnetic fields on collagen synthesis in rat skin." *Biotechnol Appl Biochem* 43, 71-75, 2006

[40] Guler G., Hardalac F., and Arıcıoglu A., "Examination of Electric Field Effects on Lipid Peroxidation and Antioxidant Enzymes by Using Multilayer Perceptron Neural Network," *G. U. Journal Science*, **18**, pp. 27-37, 2005.

[41] Guler G., Hardalac F., and Arıcıoglu A., "Examination of Electric Field Effects on Tissues By Using Back Propagation Neural Network," *Journal of Medical Systems* 29: 679-708, 2005.

[42] Guler G., and Hardalac F., "Examination of Electric field effects on oxidant and antioxidant enzymes by using hybrid genetic algoritm and neural network," IFMBE Proc 3rd European Medical&Biological Engineering Conference - EMBEC´05. Prague, Czech Republic, vol. 11, pp: 1220-1224, Nov. 20-25, 2005

[43] Canseven A.G., Seyhan N., "Design, Installation and Standardization of Homogenous Magnetic Field Systems For Experimental Animals." *The 3rd European Medical and Biological Engineering Conference EMBEC'05,* Prague, Czech Republic, 20-25 November 2005

[44] Woessner JF., "The Determination of Hydroxyproline in Tissue and Protein Samples Containing Small Proportions of This Iminoacid." *Arch Biochem Biophys* 93 : 240-247, 1961.

[45] Hecht-Nielsen, R., *Neurocomputing*, Addison-Wesley, Reading, MA.,1990

[46] Rumelhart, D.E, Hinton, G.E., Williams, R.J., "Learning internal representation by error propagation." In: Rumelhart, D.E., McClleland, J.L. (Eds.). *Parallel Distributed Processing: Exploration in the Microstructure of Cognition,* Vol. 1. MIT Press, Cambridge, MA, Chapter 8., 1986

[47] Cevik, A., *A new approach for elostoplastic analysis of structures:Neural networks.* Ph. D. Thesis, University of Gaziantep, 2006

[48] Guzelbey I.H., Cevik A. and Gögüş M.T., "Prediction of rotation capacity of wide flange beams using neural networks," *Journal of Constructional Steel Research,* Vol. 62 (10), pp. 950-96, 2006

[49] Cevik A. and Guzelbey I.H., "A soft computing based approach for the prediction of ultimate strength of metal plates in compression," *Engineering Structures,* In Press, Available online 30 June 2006.

Ayse G CANSEVEN is Assist. Prof. Dr. in Biophysics Department at Gazi University Faculty of Medicine, Vice Director GNRP -Gazi Non-Ionizing Radiation Protection- Center, Ankara, TURKEY BSc degree from Middle East Technical University, Department of Electric and Electronic Engineering, MSc and PhD degrees from Biophysics Department in Medical Faculty. Scientific interests: Electromagnetic fields - tissue interaction and interaction mechanisms, biological effects of ELF magnetic field, dosimetry, safety levels for non-ionising radiation and biological effects of RF / MW fields.

Gülay TOHUMOGLU received the B.S, the M. S and Ph. D. degrees in Electrical and Electronics Eng Dept of Middle East Technical University (METU), Turkey, in 1983, 1986, and 1993, respectively. In 1983, she joined the METU, Gaziantep campus as a research assistant and she became an Assist. Prof. at the University of Gaziantep in 1993. She had been Universidad Polytechnica de Madrid, Spain as a visiting researcher in 1996. She is currently Head of the department of Electrical and Electronics Engineering at the University of Gaziantep. Her research interests include analysis of linear and nonlinear systems, periodically time-varying systems, (neuro-fuzzy) control systems. In recent years, she has oriented her interests into the (biomedical) signal and image processing.

Abdulkadir CEVIK, received his Eng Degree in Civil Engineering in 1994 from METU in Ankara,TURKEY. He received his Master Degree in the same department in 1998 from Construction Mangement Division. He received PhD degree in University of Gaziantep at Mechanical Engineering Department from Mechanics Division in 2006. His research interests are soft computing applications (Neural Networks, Genetic Programming, Fuzzy Logic, Multivariate Regression).

Nesrin SEYHAN has completed her university education in Physics and Computer Engineering at the Middle East Technical University (METU), Ankara, Turkey. She received her Ph.D. degree in Biophysics. She is the head of Biophysics Department and Bioelectromagnetics Laboratory at Gazi University in Ankara since 1990. She has initiated M.Sc. and Ph.D. degree programs in Biophysics at the same university. She has been the founder and director of Gazi Non-Ionizing Radiation Protection (GNRP) Center. Her research interests are non-ionizing radiation sources, standards and measurements, biological effects of ELF and RF EMF including lipid peroxidation, immune system and collagen synthesis. She has been the National Representative of WHO EMF International Advisory Committee since 2001. She is the author and co-author of two books and she has published 40 research articles.

FIGURES

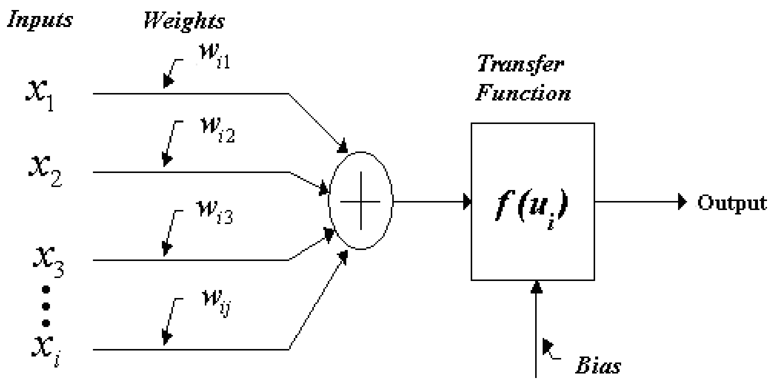

Figure 1. *Basic Elements of an Artificial Neuron .*

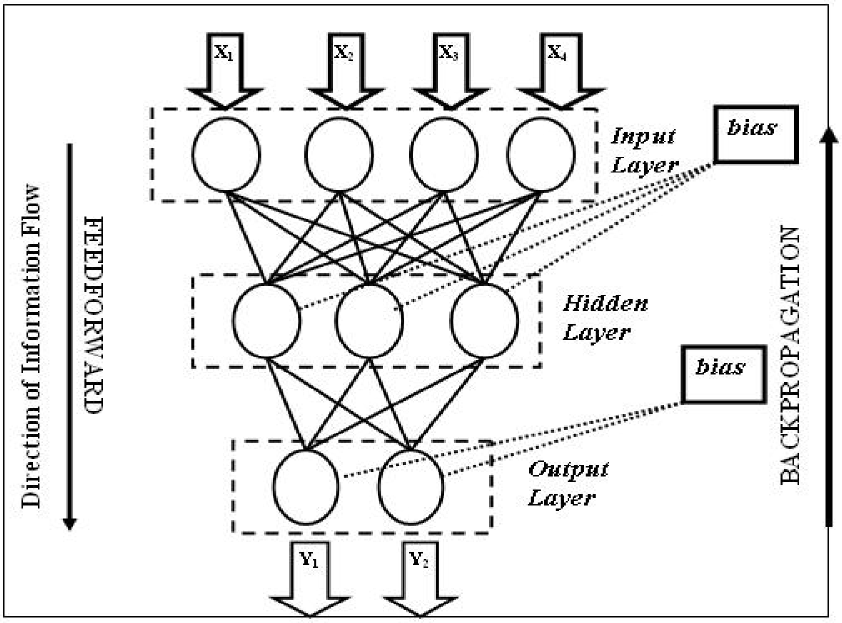

Figure 2. *Backpropagation Algorithm*

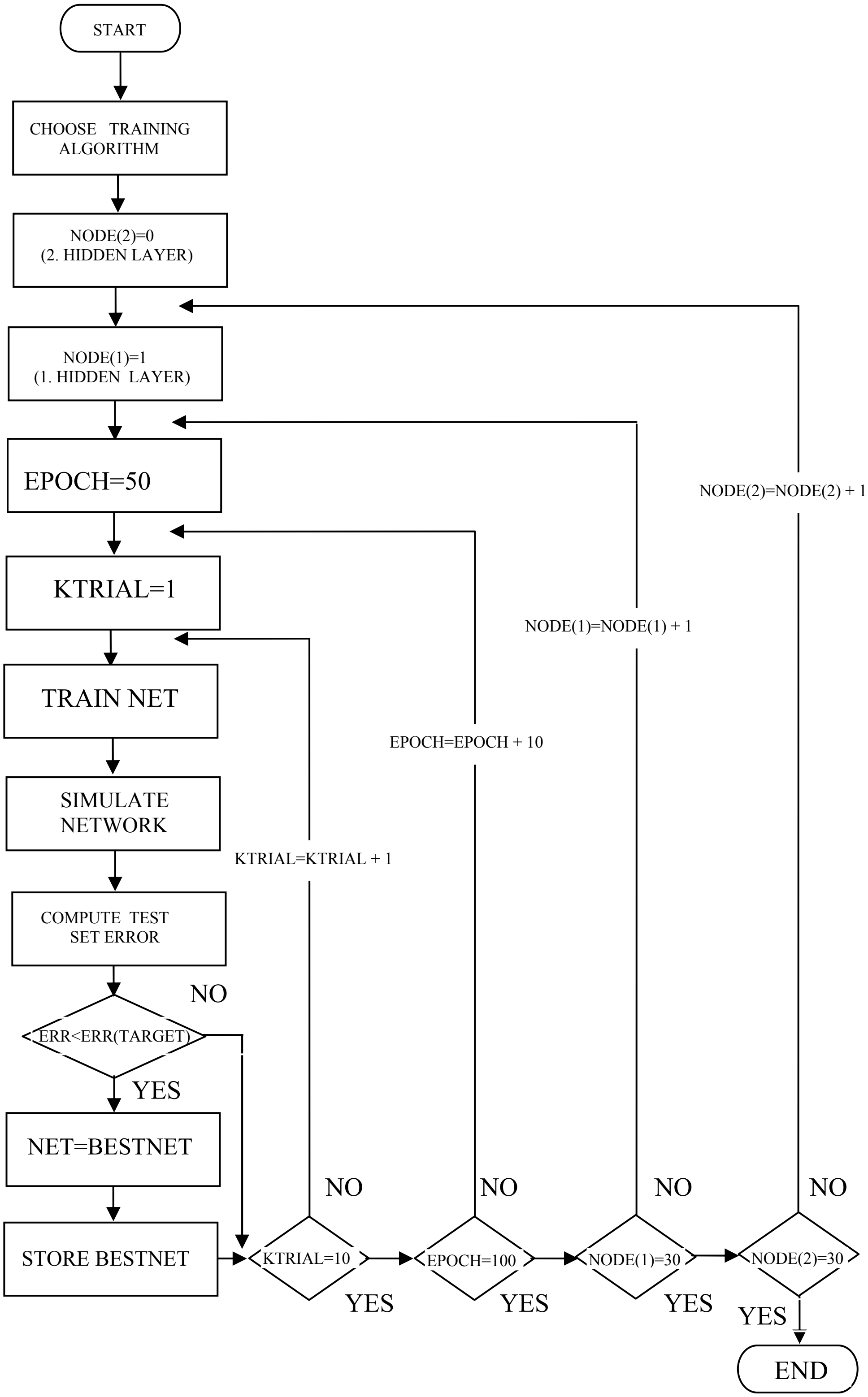

Figure 3. *The flowchart of the whole selection process*

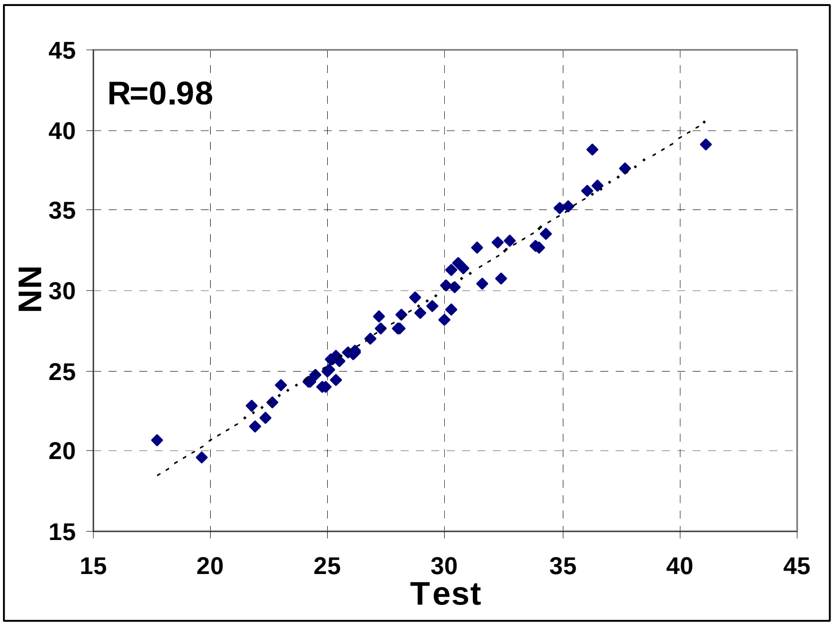

Figure 4. *Performance of NN vs Test Results*

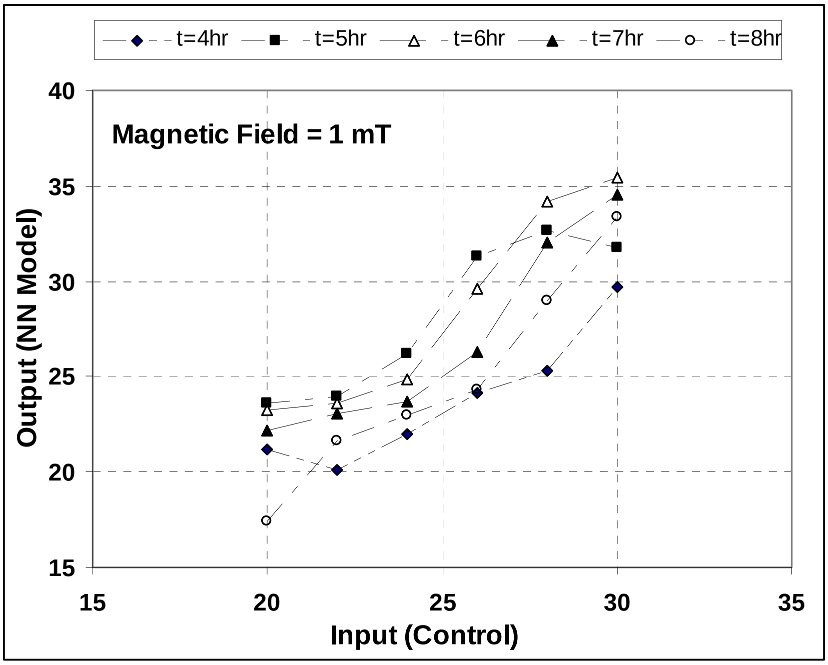

Figure 5. *Influence of time to hydroxyproline output (Magnetic Field = 1 mT)*

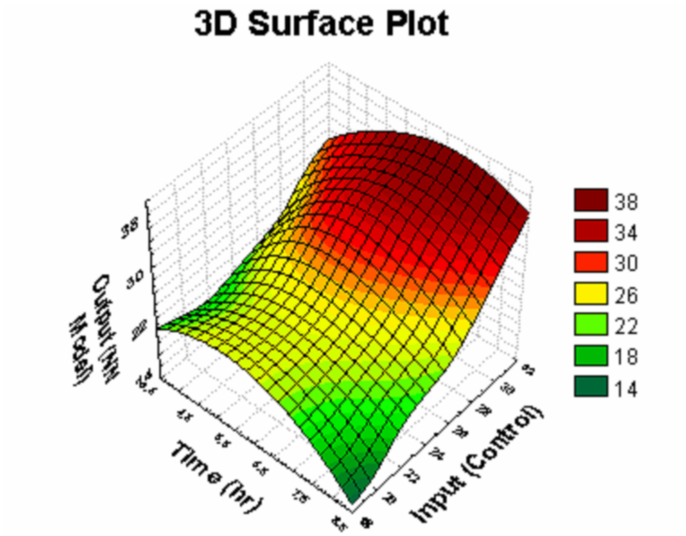

Figure 6. *3D Surface plot of Influence of time to hydroxyproline output (Magnetic Field = 1 mT)*

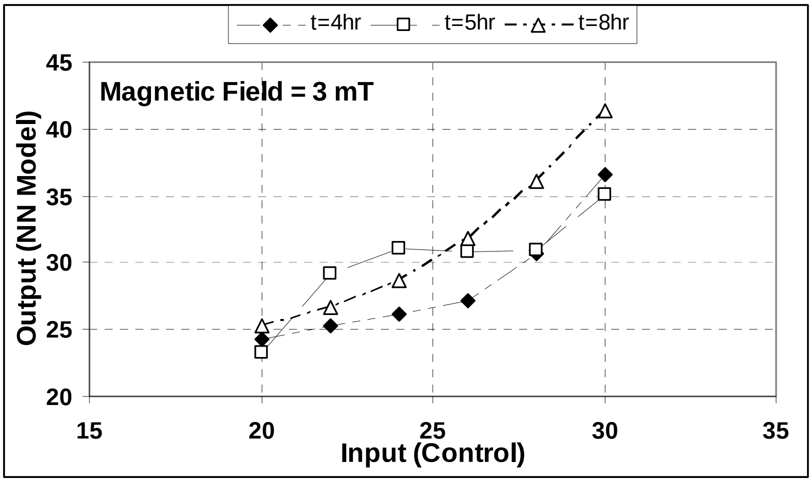

Figure 7. *Influence of time to hydroxyproline output (Magnetic Field = 3 mT)*

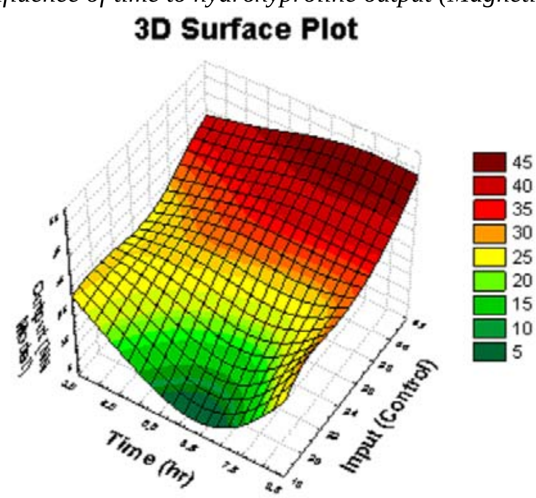

Figure 8. *3D Surface plot of Influence of time to hydroxyproline output (Magnetic Field = 3 mT)*

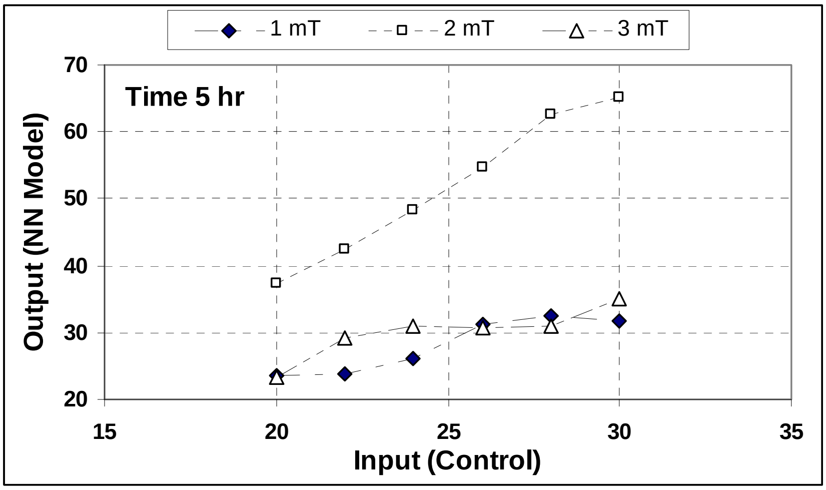

Figure 9. *Influence of EMF to hydroxyproline output (Time Duration= 5hr)*

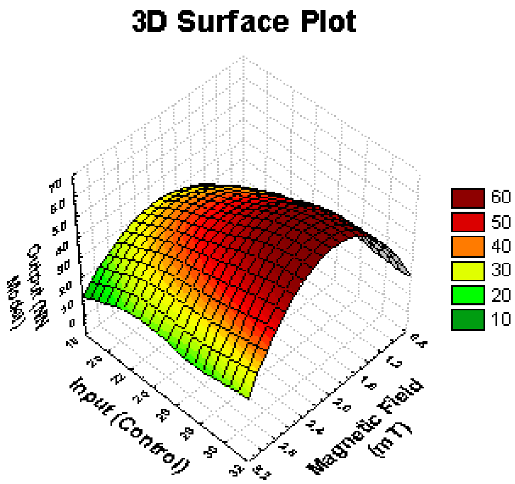

Figure 10. *3D Surface plot of Influence of EMF to hydroxyproline output (Time Duration= 5hr)*

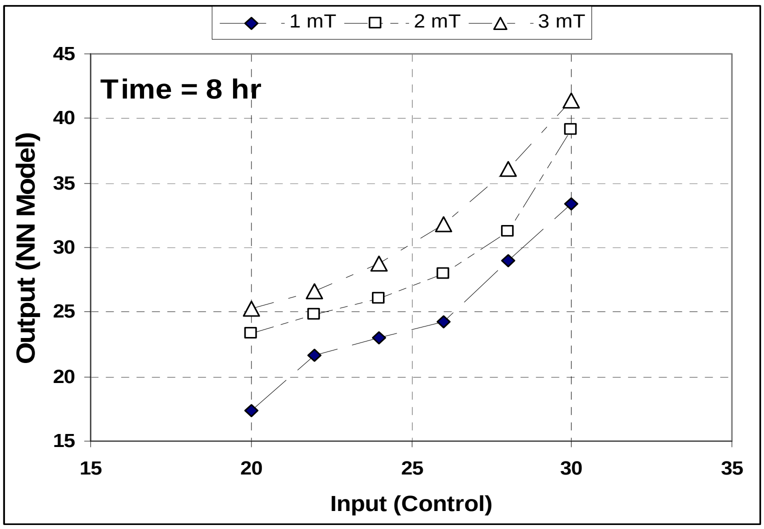

Figure 11. *Influence of EMF to hydroxyproline output (Time Duration= 8hr)*

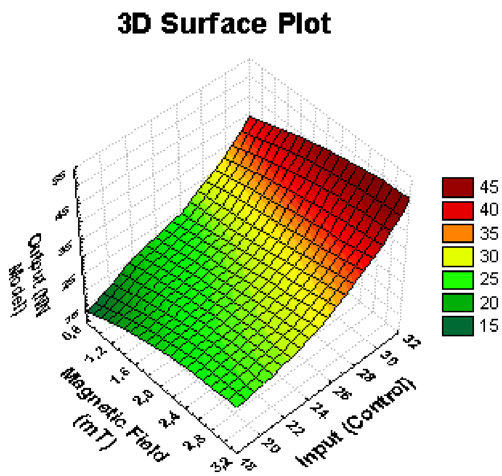

Figure 12. *3D Surface plot of Influence of EMF to hydroxyproline output (Time Duration= 8hr)*

TABLES

Table 1. Skin hydroxyproline content of field-exposed groups with respect to controls

Groups (n=9)	**Hydroxyproline* (mg/g wet weight)**	**Statistics**
Controls	25.65 ± 2.46	
1 mT/4 hours	23.38±2.60	p=0.0576, p>0.05
1 mT/8 hours	25.00±3.76	p=0.5078, p>0.05
2 mT/4 hours	34.25±3.50	p=0.0003, p<0.001
2 mT/8 hours	28.15 ±2.46	p=0.077, p>0.05
3 mT/4 hours	28.13±2.88	p=0.122, p>0.05
3 mT/8 hours	31.90 ± 4.10	p=0.0041, p<0.005

(*) x ± sd: mean ± standard deviation

Table 2. *Results of NN model vs Experimantal results*

* Bold sets are test sets

Magnetic Field (50 Hz)	Time (hr)	Control Group	TEST	NN	TEST/NN
1	**4**	**20.74**	**17.75**	**20.69**	**0.86**
1	4	23.74	21.90	21.53	1.02
1	4	24.08	22.32	22.12	1.01
1	4	25.75	23.00	24.08	0.96
1	4	26.45	24.15	24.33	0.99
1	4	26.50	24.23	24.35	1.00
1	4	26.83	25.35	24.47	1.04
1	**4**	**28.20**	**25.50**	**25.56**	**1.00**
1	4	28.62	26.15	26.21	1.00
1	8	20.74	19.65	19.62	1.00
1	8	23.74	21.73	22.86	0.95
1	8	24.08	22.61	23.01	0.98
1	8	25.75	24.76	24.01	1.03
1	8	26.45	24.99	24.93	1.00
1	**8**	**26.50**	**25.02**	**25.02**	**1.00**
1	8	26.83	25.13	25.67	0.98
1	8	28.20	28.71	29.56	0.97
1	8	28.62	32.37	30.79	1.05
2	4	20.74	30.00	30.37	0.99
2	4	23.74	30.37	30.26	1.00
2	4	24.08	31.56	30.43	1.04
2	**4**	**25.75**	**32.74**	**33.11**	**0.99**
2	4	26.45	34.91	35.13	0.99
2	4	26.50	35.28	35.27	1.00
2	4	26.83	36.03	36.21	1.00
2	4	28.20	36.25	38.79	0.93
2	4	28.62	41.14	39.16	1.05
2	8	20.74	24.89	23.97	1.04
2	**8**	**23.74**	**25.34**	**25.91**	**0.98**
2	8	24.08	25.88	26.16	0.99
2	8	25.75	27.98	27.65	1.01
2	8	26.45	28.16	28.50	0.99
2	8	26.50	28.96	28.56	1.01
2	8	26.83	29.46	29.03	1.01
2	**8**	**28.20**	**30.52**	**31.76**	**0.96**
2	8	28.62	32.25	33.01	0.98
3	4	20.74	24.49	24.76	0.99
3	4	23.74	26.11	26.00	1.00
3	4	24.08	26.16	26.14	1.00
3	4	25.75	26.79	27.00	0.99
3	4	26.45	27.28	27.64	0.99
3	4	26.50	28.04	27.70	1.01

3	**4**	**26.83**	**29.97**	**28.13**	**1.07**
3	4	28.20	30.26	31.27	0.97
3	4	28.62	34.03	32.64	1.04
3	8	20.74	25.21	25.68	0.98
3	8	23.74	27.21	28.38	0.96
3	8	24.08	30.25	28.81	1.05
3	**8**	**25.75**	**30.77**	**31.40**	**0.98**
3	8	26.45	31.38	32.72	0.96
3	8	26.50	33.87	32.82	1.03
3	8	26.83	34.27	33.49	1.02
3	8	28.20	36.50	36.56	1.00
3	**8**	**28.62**	**37.65**	**37.61**	**1.00**
				MEAN	**1.00**
				STD DEV	**0.03**
				R	**0.98**

Table 3. *Statistical Parameters for NN Model*

	MAPE (%)	**Mean** (Test / NN)	**Std Dev**	**R** (Correlation oeeffient)
Test set	3.37	0.98	0.051	0.978
Train Set	2.13	1.00	0.027	0.984

(**MSE**: Mean Squared Error, **RMSE**: Root Mean Squared Error, **SSE:** Sum of Squared Error**,** **MAPE**: Mean Absolute Percentsge Error)