EXAMINATION OF ELECTRIC FIELD EFFECTS ON OXIDANT AND ANTIOXIDANT ENZYMES BY USING HYBRID GENETIC ALGORITM AND NEURAL NETWORK

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Abstract: The aim of this study is to determine lipid peroxidation and antioxidant enzyme levels in spleen tissue of guinea pigs which were exposed to different intensities static electric fields. And the experimental results are applied to hybrid genetic algorithm and neural networks as learning data and the training of the feed forward neural network is realized. At the end of this training; without applying electric field to tissues, the determination of the effects of the electric field on tissues by using computer is predicted by the neural network.

Introduction

The participation of free radical biochemistry in several pathologies and aging has been demonstrated. Free radicals, such as superoxide anions (O_2^{\bullet}) , which are generated by the electrical stimulus show high chemical reactivity and as a result have a relatively short lifetime in the free state [1-4]. The free radical oxidation of polyunsaturated fatty acids in biological systems is known as lipid peroxidation and the detection and measurement of lipid peroxidation is the evidence most frequently cited to support the involvement of free-radical reactions [5]. The increase in radicals can be traced to the variation in malondialdehyde (MDA) quantities, which is an end product of lipid peroxidation [6].

The importance of the ensyme, superoxide dismutase (SOD), in eliminating these radicals is well established [7-8]. Superoxide dismutase scavenges the superoxide radicals by catalyzing the reactive O_2 ^{*} species into dioxygen and oxygen peroxide, thereby protecting cells against the reactive oxygen species produced by the electric field or other mechanisms [9,10].

This study investigated the changes in MDA and SOD levels due to the effects of static electric fields in guinea pigs and the experimental results were applied to hybrid genetic algorithm and neural networks (GANN) as learning data and the training of the feed forward neural network has been realized. At the end of this training, to determine the effect of the electric field on tissues in computer, without applying electric field to tissues and without using too many guinea pigs and to

form a database for the researchers in this field are aimed.

Materials and Methods

Electric Field Exposure: Electric potentials were applied to the copper plates mounted on the wooden boxes to produce electric fields with magnitudes of 0.3 kV/m, 0.6 kV/m, 0.8 kV/m, 0.9 kV/m, 1 kV/m, 1.35 kV/m, 1.5 kV/m, 1.8 kV/m and 1.9 kV/m. Male white guinea pigs (150-200 g) were continuously exposed to electric fields for 8 hours per day over 3 days (Table 1). Each group of 20 guinea pigs was exposed to the electric field from 9 a.m. to 5 p.m. Twenty guinea pigs were used as controls and were kept under the same conditions without being exposed to any electric field. Animals were housed in cages for 3 days.

*Malondialdehyde Analysis***:** The effects of electric fields on lipid peroxidation are found by determining the level of malondialdehyde (MDA) in spleen tissue [11].

Superoxide Dismutase Analysis : The effects of electric fields on antioxidant enzymes are found by determining the level of SOD in spleen tissue [12,13].

Neural Network: Neural networks are a form of artificial intelligence that consist of nonlinear computer algorithms that ''learn'' with feedback to reproduce the existing relationship between input and output variables of complex nonlinear systems [14]. Back propagation is currently the most widely used supervised learning algorithm in neural network applications. Its popularity can be attributed primarily to the fact that this algorithm, in conjunction with three layer feed forward architecture is capable of approximating to any degree if accuracy, any reasonable arbitrary nonlinear inputoutput mapping, provided that the neural network has a sufficient number of hidden units.

Hybrid Genetic Algorithm and Neural Network Approach: Genetic algorithms are stochastic optimization algorithms which have proved to be effective in various applications. A typical genetic algorithm maintains a population of solutions and implements a 'survival of the fittest' strategy in the search for better solutions. It has been shown to be capable of finding global optima in complex problems by exploring virtually all regions of the state space and exploiting promising areas through mutation, crossover and selection operations applied to individuals in the populations. Genetic algorithms apply selection, crossover and mutation operators to construct fitter solutions. A genetic algorithm processes populations of chromosomes by replacing unsuitable candidates according to the fitness function. The fitness function determines how well the processed chromosome solves the problem [15]. In this study a genetic algorithm is used to obtain near-optimal neural network structure.

The Evaluation of the Hybrid GANN : In experiments, back propagation and momentum are used together and tangent hyperbolic (tanh) is selected as the function of transfer. Rather than to determine a fixed MSE value as the stopping criterion, the number of steps in the experiment is fixed and the learning is realized within 1000 steps. The crossover and mutation probabilities which are the genetic algorith parameters found as 0.9 and 0.1, respectively. In addition, we started with a population of 50 random networks, and evolved these networks through 100 generations.

The Evaluation of Electric Field Data in The Hybrid GANN: In this study MDA and SOD results belonging to spleen tissue of guinea pigs exposed for 3 days to electric fields in the strength of 0.3 kV/m, 0.6 kV/m, 0.8 kV/m, 0.9 kV/m, 1 kV/m, 1.35 kV/m, 1.50 kV/m, 1.8 kV/m and 1.9 kV/m are evaluated, and input and output vectors are formed for the results of this experiment to be learned by the hybrid GANN. Each input vector is composed of x_1 = the measure result of control. As outputs of input vector applied, the measure results in the strength of electric field belonging to $y_1 = 0.3$ kV/m, $y_2 = 0.6$ kV/m, *y3* = 0.8 kV/m, *y4* = 0.9 kV/m, *y5* = 1 kV/m, $y_6 = 1.35$ kV/m, $y_7 = 1.50$ kV/m, $y_8 = 1.8$ kV/m and $y_9 = 1.9$ kV/m are defined as output vector.

Results

Group I : Some of the experiment results belonging to SOD data of spleen tissue of electric fields applied in different intensities are shown in Table 2. The minimum error value (MSE) obtained is 0.1002. As it is seen in Figure 1, the learning error reached approximately to 0.1002 at the $63th$ generation, and the learning was completed successfully in the 100th generation.

After the learning had been completed successfully (MSE <0.1004), real experiment results (Table 2) were compared with experiment results which were predicted by the hybrid GANN (Table 3). The prediction performance obtained after the comparison is computed as seen in Table 4. The prediction performance was 99.98% in 0.3 kV/m, 99.98 % in 0.6 kV/m, 99.98 % in 0.8 kV/m, 100.00 % in 0.9 kV/m, 99.99 % in 1 kV/m, 99.99 % in 1.35 kV/m, 100.00% in 1.50 kV/m, 99.99 % in 1.8 kV/m and 100.00 % in 1.9 kV/m. Thus a prediction performance of 99.99 % (general average) is obtained.

Group II: Some of the experiment results belonging to MDA data of spleen tissue of electric fields applied in different intensities are shown in

Table 5. The minimum error value (MSE) obtained is 0.1305. As it is seen in Figure 2, the learning error reached approximately to 0.1305 at the $5th$ generation, and the learning was completed successfully in the $100th$ generation.

After the learning had been completed successfully (MSE <0.131), real experiment results (Table 5) were compared with experiment results which were predicted by the hybrid GANN (Table 6). The prediction performance obtained after the comparison is computed as seen in Table 7. The prediction performance was 99.88% in 0.3 kV/m, 99.88 % in 0.6 kV/m, 99.91 % in 0.8 kV/m, 99.03 % in 0.9 kV/m, 99.20 % in 1 kV/m, 98.81 % in 1.35 kV/m, 99.56% in 1.50 kV/m, 99.53 % in 1.8 kV/m and 99.59 % in 1.9 kV/m. Thus a prediction performance of 99.49 % (general average) is obtained.

Discussion

In the study of electric field applied different intensities, 99.99 % of the average prediction performance of the hybrid GANN of experiment data belonging to Group I; 99.49 % of the average prediction performance of the hybrid GANN of experiment data belonging to Group II.

Those percentiles of the prediction performance of the hybrid GANN belonging to experiment results of electric field were so high; this fact shows that the hybrid GANN which are used many fields could be applied in the studies of electric field too. Furthermore this study may form a database for the scientists investigating the effects of electric fields on lipid peroxidation and antioxidant enzymes.

In our future studies which will investigate the health effects of electric and magnetic fields on different parameters, it is aimed to determine the biological effects of these fields by using computer and the hybrid GANN and without using too many guinea pigs.

References

- [1] EBEIGBE A.B., GANTZOS R.D., AND WEBB R.C. (1983): 'Relaxation of Rat Tail Artery to Electrical Stimulation', *Life Sci.*, 33, pp 303-309.
- [2] GREENBERG B., RHODEN K., AND BARNES P.J. (1986): 'Activated Oxygen Molecules Generated by Electrical Stimulation Affect Vascular Smooth', *Muscle. J. Mol. Cardiol.*, 18, pp 975-981.
- [3] HULSMANN A.R., RAATGEEP H. R., GARRELD I.M., TOORENENBERGEN A.W.M., AND JONGSTE J.C. (1993): 'Electrical Field Stimulation Causes Oxidation of Exogenous Histamine in Krebs-Henseleit Buffer: A Potential Source of Error in Studies of Isolated Airways', *JPM*, 30, pp 149- 152.
- [4] LAMB F.S., AND WEBB R.C. (1984): 'Vascular Effects of Free Radicals Generated by Electrical Stimulation', *Am. J. Physiol.* , 247, pp H709- H714.
- [5] GUTTERIDGE J.M.C. (1995): 'Lipid Peroxidation and Antioxidants as Biomarkers of Tissue Damage', *Clin. Chem.*, 41, pp 1819-1828.
- [6] MACCALL J.M., BRAUGHLER J.M., AND HALL E.D. (1987): 'Lipid Peroxidation and the Role of Oxygen Radicals in CNS Injury', *Acta. Anaesth. Belg.,* 38, pp 373-379.
- [7] DESIDERI A., FALCONI M., POLTICELLI F., BOLOGNESI M., DJNOVIC K., AND ROTILIO G. (1992): 'Evolutionary Conservativeness of Electric Field in the Cu,Zn Superoxide Dismutase Active Site, Evidence for Co-Ordinated Mutation of Charged Amino Acid Residues', *J. Mol. Biol.*, 223, pp 337-342.
- [8] SALO D.C., PACIFICI R.E., LIN S.W., GIULIVI C., AND DAVIES K.J.A. (1990): 'Superoxide Dismutase Undergoes Proteolysis and Fragmentation Following Oxidative Modification and Inactivation', *J. Biol. Chem.*, 265, pp 11919- 11927.
- [9] BENOV L.C., ANTONOV P.A., AND RIBAROV S.R. (1994): 'Oxidative Damage the Membrane Lipids after Electroporation', *Gen. Physiol. Biophys.,* 13, pp 85-97.
- [10] SCAIANO J.C., MOHTAT N., COZENS F.L., MCLEAN J., AND THANSANDOTE A. (1994): 'Application of the Radical Pair Mechanism to Free Radicals in Organized Systems: Can the Effects of 60 Hz Predicted from Studies under Static Fields ?', *Bioelectromagnetics*, 15, pp 549-554.
- [11] WASOWICS W., NEVE S., AND PERETZ A. (1993): 'Optimized Steps in Fluorometric Determination of Thiobarbituric Acid Reactive Substances in Serum: Importance of Extraction pH and Influence of Sample Preservation and Storage', *Clin. Chem.*, 39, pp 2522-2526.
- [12] LOWRY O.H., ROSEBROUGH N.I., FARR A.L. AND RANDALL R.J. (1951): 'Protein Measurement with the Folin Phenol Reagent', *J. Biol. Chem.* , 193, pp 265-275.
- [13] SUN Y., OBERLEY L.W. AND LI Y. (1988): 'A Simple Method for Clinical Assay of Superoxide Dismutase', *Clin. Chem.,* 34, pp 497-500.
- [14] BISHOP C.M. (1995): 'Neural Network for Pattern Recognition', Oxford University Press, New York.
- [15] GOLDBERG D. (1989): 'Genetic Algorithms in Search, Optimization, and Machine Learning', Addison-Wesley, Reading, MA.

Figure 1: The Fitness Variation Belonging to SOD Data of Spleen Tissue

Figure 2: The Fitness Variation Belonging to MDA Data of Spleen Tissue

Table 1: Working Groups Belonging to Data of Electric Field Applied Different Intensities

Table 2: Real Experiment Results Belonging to Group I

Table 3: Experiment Results of Group I; These Results were Predicted by the Neural Network.

т	1	2	3	4	5
$\mathbf C$	8.33000	8.3200	8.31000	8.30000	8.29000
A	8.34699	8.3475	8.34840	8.34466	8.35007
B	8.38600	8.3885	8.39020	8.38832	8.38514
D	8.55800	8.5610	8.56020	8.56000	8.56000
E	10.18850	10 189	10.19040	10 19067	10.19201
F	10.19300	10.195	10.19520	10.19467	10.19400
G	14.01100	14.014	14.01320	14.01367	14.01300
H	14.09200	14.089	14.08920	14.09200	14.09002
T	14.54850	14.550	14.55120	14.55033	14.55100
J.	14.55550	14.556	14.55440	14.55567	14.55500

Table 4: The Prediction Performance Belonging to Group I

E.N : Experiment Number; **C:** Control; **A:** 0.3 kV/m; **B:** 0.6 kV/m; **D:** 0.8 kV/m;**E:** 0.9 kV/m; **F:** 1kV/m; **G:** 1.35 kV/m; **H**: 1.5 kV/m; **I:** 1.8 kV/m; **J**: 1.9 kV/m;

T : Test Number; **C:** Control; **A:** 0.3 kV/m; **B:** 0.6 kV/m; **D:** 0.8 kV/m;**E:** 0.9 kV/m; **F:** 1kV/m; **G:** 1.35 kV/m; **H**: 1.5 kV/m; **I:** 1.8 kV/m; **J**: 1.9 kV/m;

Table 5: Real Experiment Results Belonging to Group II

E.N	1	$\mathbf{2}$	3	4	5
C	0.0881	0.0883	0.0882	0.0880	0.0883
A	0.0888	0.0889	0.0890	0.0891	0.0891
B	0.0896	0.0897	0.0897	0.0895	0.0896
D	0.0899	0.0899	0.0899	0.0897	0.0901
E	0.1120	0.1120	0 1 1 4 0	0 1 1 4 0	0.1140
F	0.1180	0.1180	0.1180	0.1160	0 1 1 6 0
G	0.1630	0.1630	0.1620	0.1630	0.1620
Н	0.1650	0.1670	0.1660	0.1650	0.1650
I	0.1820	0.1830	0.1820	0.1800	0.1820
J	0.1840	0.1860	0.1850	0.1860	0.1850

Table 6: Experiment results of Group II; these results were predicted by the neural network.

т	1	$\mathbf{2}$	3	4	5
$\mathbf C$	0.08810	0.08830	0.08820	0.08800	0.08830
A	0.08906	0.08903	0.08905	0.08907	0.08903
B	0.08952	0.08951	0.08952	0.08952	0.08951
D	0.08981	0.08990	0.08985	0.08978	0.08990
E	0.11249	0.11326	0.11291	0.11207	0.11326
F	0.11749	0.11731	0.11740	0.11757	0.11731
G	0.16031	0.16113	0.16065	0.16011	0.16113
H	0.16561	0.16562	0.16561	0.16564	0.16562
I	0.18167	0.18158	0.18164	0.18169	0.18158
J	0.18547	0.18572	0.18562	0.18530	0.18572

Table 7: The prediction performance belonging to Group II.

E.N : Experiment Number; **C:** Control; **A:** 0.3 kV/m; **B:** 0.6 kV/m; **D:** 0.8 kV/m; **E:** 0.9 kV/m; **F:** 1kV/m; **G:** 1.35 kV/m; **H**: 1.5 kV/m; **I:** 1.8 kV/m; **J**: 1.9 kV/m;

T : Experiment Number; **C:** Control; **A:** 0.3 kV/m; **B:** 0.6 kV/m; **D:** 0.8 kV/m;**E:** 0.9 kV/m; **F:** $1kV/m$; **G:** 1.35 kV/m; **H**: 1.5 kV/m; **I:** 1.8 kV/m; **J**: 1.9 kV/m;