Determination Of Long-Term Outcome In Patients With Coronery Artery Disease Using An Artificial Neural Network

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ABSTRACT
Echocardiography is making tremendous strides and as such various guidelines and position papers are regularly being published still competency and knowledge updating of all concerned is key requirement. In face of uncertainty of disease symptoms even experienced cardiologists need complimentary assistance from intelligent decision system to arrive at precise diagnosis of cardiac diseases. This research work is aimed at developing it using neural network approach. This study sought to assess the usefulness and accuracy of artificial neural networks (ANN) in the Echocardiographic view classification of the patient's survival and death in patients with heart failure. Paper discusses performances of self organizing feature map (SOFM) and Jordan neural network (JORDAN NN) approaches for classification on two different data sets (unseen data). SOFM NN approach gives the best results over JORDAN NN, and outperforms in various performance measures, such as accuracy (100% correct detection, only 0.92 % error in multifold cross validation). Detailed design procedure for achieving the optimal NN model and Principal Component Analysis for dimensionality reduction is proposed.

Categories and Subject Descriptors

D.3.3 [**Programming Languages**]: Language Contructs and Features – *abstract data types, polymorphism, control structures.*

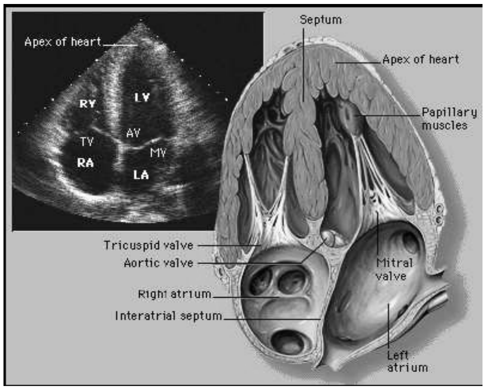
General Terms

Algorithms, Performance, Design, Experimentation, Verification

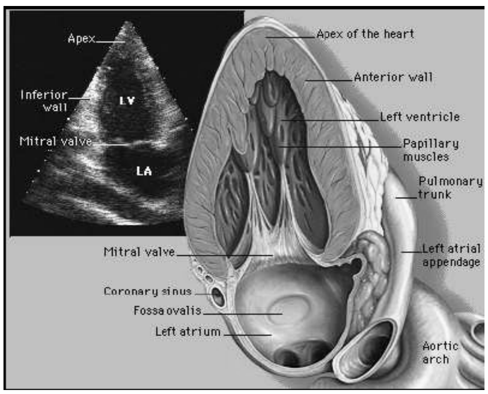
Keywords
Neural computation in Medicine, Echocardiogram, Cross Validation, SOFM, JORDAN NN, Classification

1 INTRODUCTION
Artificial neural networks are computational techniques used to represent and process information by means of networks of interconnected processing elements, similar to neurons. They have found applications in medical decision support systems, particularly in prognosis. In the apical four chambers (A4C) view shown in Figure 1(a), all four cavities, namely left and right ventricles, and left and right atria, are present. In the apical two-chamber (A2C) view shown in Figure 1(b), only the left ventricle and the left atrium are present. The Figure 1 (a, b and c) shows a snapshot taken during an echocardiogram. The echocardiograhy is widely used to assess cardiovascular functionalities such as valvular regurgitation and stenosis [Otto C. M.]. It is captured by an ultrasound transducer that employs the Doppler Effect to determine whether blood is moving towards or away from the ultrasound probe, and its relative velocity [Tei and Schiller].

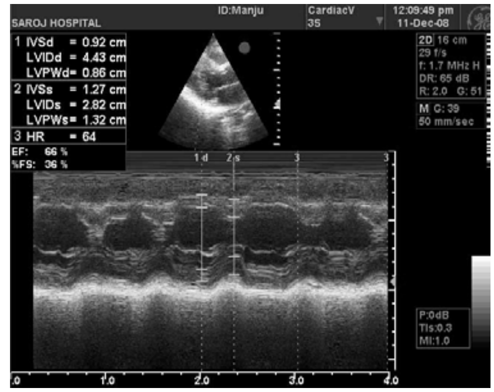
1.1 Clinical Data Set
Clinical and Doppler-derived Echocardiographic data from 62 consecutive patients with diffuse impairment of myocardial contractility were studied. After 1 year, data regarding survival (18 Survived) or death (44 Deaths) were obtained and produced the prognostic variable. The data base was divided randomly into a training data set (16 survival, 40deaths) and an unknown testing data set (02 survival, 04deaths). Results of two artificial neural networks, SOFM NN and JORDAN NN models are compared. The particular databases chosen for this; have numerical attributes, since we have been focusing on learning for numeric data using Echocardiogram Database [Murphy]. This data set contains echocardiogram data on a group of people who have had heart attacks in the past. The objective of this data set is to try to use features of an echocardiogram (such as "left ventricular end diastolic dimension" and "E-point septal separation") to predict whether a person will still be living a year after their heart attack, based on features of the echocardiogram [Zhou]. Data set contains 62 instances and 08 attributes. As an implementation example, a dataset is classified by SOFM NN and JORDAN networks and the real performances of these networks are found by applying ROC analysis. The use of relative operating characteristic (ROC) curves in test performance evaluation is done to calculate this fitness function; the methodology is able to optimize classifier performance in domains with non-uniform class distribution [Tokan]. In order to make objective assessment of classifier quality, we used average class accuracy, which on unbalanced data sets is more informative measure than overall accuracy. Table 1 shows the related research [Tsai, Brotherton, Panayiotu, Zhou, Johansson, Hikawa and Reyneri]. Neuro Solutions (version 5.7) [Neuro Dim. Inc.] and MATLAB (version 8.0) are specifically used for obtaining results [Math work inc.]. An exhaustive and careful experimental study has been carried out to determine the optimal configuration.



(a)



(b)



(c)

Figure 1. The illustration of (a) Apical four-chamber (A4C), (b) Apical two-chamber (A2C) views. Image source: Yale Atlas of Echo. (c) 2D Doppler Echocardiogram.

1.2 Scatter Plots

Typical scatter plots for survival and not survival classes are depicted below in Figure 2 which clearly demonstrates the overlapping and complications in discrimination. Estimation of appropriate decision boundaries in order to discriminate different classes precisely is indeed a challenging task in the light of partial overlapping among the classes. In addition to this, the clusters make the classification problem more difficult and complex. To solve it efficiently, neural networks are used as classifiers.

Table 1. Related Research

Researchers	Data Base	Technique	Results
Nicholas Andrisevic, Khaled Ejaz, Fernando Rios-Gutierrez, and Rocio Alba-Flores (2005)	Department of Family Medicine, University of Minnesota School of Medicine Duluth	Principal Component Analysis	specificity 70.5% sensitivity 64.7%
Du-Yih Tsai	Gifu University School of Medicine	Genetic Algorithms	81%
Tom Brotherton, Tom Pollard, Pat Simpson, and Anthony DeMaria	University of California at Irvine Machine Learning Repository	Fuzzy Min-Max	% Correct 87% SD ±7%
Panayiota Poirazi, Costas Neocleous, Costantinos S. Pattichis	University of California at Irvine Machine Learning Repository	Modular Neural Network	% Correct 89% SD ±6.88%
Kevin Zhou S. , Park J.H., Georgescu B., Simopoulos	Ultrasound Division, Siemens Medical	Logit Boosting algorithm	% Correct 90% SD ±8.88%
Jaurez O.M.	M mode 2Dimensional Doppler examinations	Neural Networks	Accuracy 90% Specificity 93% Sensitivity 71.4%

2 DESIGN OF INTELLIGENT SYSTEM

There are numerous neural networks structures reported in the literature but most of them are highly application specific.

2.1 Self Organizing Feature Map Neural Network

Self Organizing Feature Maps are based on competitive learning*;* the output neurons of the network compete among themselves to be activated or fired, with the result that only one output neuron, or one neuron per group, is on at any one time. An output neuron that wins the competition is called a winner-takes all neurons or simply a winning neuron. One way of inducing a winner-takes-all competition among the output neurons is to use lateral inhibitory connections (i.e., negative feedback paths) between them. In a self-organizing map, the neurons are placed at the nodes of a lattice that is usually one- or two-dimensional. Higher-dimensional maps are also possible but not as common. The neurons become selectively tuned to various input patterns (stimuli) or classes of input patterns in the course of a competitive learning process. The locations of the neurons so tuned (i.e., the winning neurons) become ordered with respect to each other in such a way that a meaningful coordinate system for different input features is created over the lattice [Princepe J.].

2.2 Jordan Neural Network

Jordan and Elman networks extend the multilayer perceptron with context units, which are processing elements (PEs) that remember past activity. Context units provide the network with the ability to extract temporal information from the data [Haykin S.]. In the Elman network, the activity of the first hidden PEs is copied to the context units, while the Jordan network copies the output of the network. Networks which feed the input and the last hidden layer to the context units are also available. The context unit controls the forgetting factor through the Time constant . Useful values are between 0 and 1. A value of 1 is useless in the sense that all of the past is factored in. On the other extreme, a value of zero means that only the present time is factored in (i.e., there is no self-recurrent connection) [Brotherton]. The closer the value is to 1, the longer the memory depth and the slower the forgetting factor. There are linear and nonlinear context units and linear and nonlinear integrators. The integrators are the same as context units except that they normalize the input based on the time constant. If there is 1 hidden layer, then the 2nd and the 3rd topologies are equivalent . Learning from the data is the essence of neuro computing. Every PE that has an adaptive parameter must change it according to some pre specified procedure. Backpropagation is by far the most common form of learning. Here it is sufficient to say that the weights are changed based on their previous value and a correction term. The learning rule is the means by which the correction term is specified [Zhou]. Once the particular rule is selected, the user must still specify how much correction should be applied to the weights, referred to as the learning rate. If the learning rate is too small, then learning takes a long time. On the other hand, if it is set too high, then the adaptation diverges and the weights are unusable. The option of MSE termination is to base the stop criteria on the cross validation set instead of the training set. As mentioned earlier, this tends to be a good indicator of the level of generalization that the network has achieved [Johansson E.M]. Increase is the default function when using the cross validation set for MSE termination. This stops the network when the MSE of the cross validation set begins to increase. This is an indication that the network has begun to over train. Overtraining is when the network simply memorizes the training set and is unable to generalize the problem. Batch learning updates the weights after the presentation of the entire training set [Hikawa H.].

2.3 Preparation of Training, Cross-Validation, and Testing Data Partitions

Table 2. Data Partition Schemes

Data Partition	Training Instances	Cross Validation Instances
Set 1(Normal Tagging)	1 to 56 (90%)	57 to 62 (10%)
Set 2(Reverse Tagging)	7 to 62 (90%)	1 to 6 (10%)

If model selection and true error estimates are to be computed simultaneously, the data needs to be divided into three disjoint sets as follows. Table 2 highlights the data partition schemes employed to design the classifier.

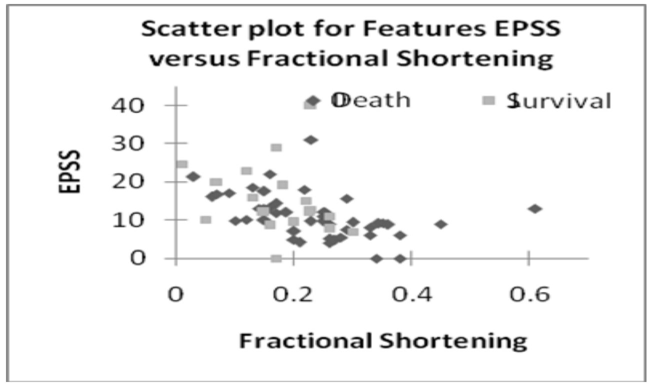


Figure 2. Scatter plot of features epss versus fractional shortening

2.4 Experimental Determination of Near Optimal SOFM NN Classifier

Since it is very likely that one ends up in a “bad” local minimum, the network should be trained a couple of times (typically 10 times), starting from different random initial weights till cross-validation error exceeds training error. All training processes automatically save the weights at the minimum cross validation, and testing data set. Details about the various training algorithms and their parameters can be found in. The choice of the optimal values was made as per the exhaustive experimentation for the training of the SOFM NN for different values of these parameters. It was found that these values of the parameters gave minimum average MSE, maximum average % classification accuracy. Variable used and optimal parameters decided are depicted in Table 3. Optimal choice of training, cross validation sets and epochs required as per cross validation based stopping criterion in supervised learning are demonstrated in Figure 3. Figure 4 shows the comparison of accuracy of the network for different transfer functions in the hidden neurons. The MSE threshold on training dataset is set to 0.01. The supervised learning may terminate earlier if the minimum specified error threshold of 0.01 is reached earlier. Figure 5 and 6 depicts that, combination of momentum learning (supervised learning rule) and Tanh transfer function in hidden and output layers have maximum accuracy and minimum MSE’s. Figure 7 illustrates weight regularization used at hidden and output layer. Regularization ratio is varied from 0.01 to 1 in increased step of 0.01. It is observed that 0.01 ratio without decay is giving best performance. Dithering is used for sensitivity analysis. All inputs are hold constant, except a particular input under observation and that input is varied from 2% to 20% with increased step of 2%. Comparison of percentage classification accuracy and MSE for % input variation is observed from Figure 8.

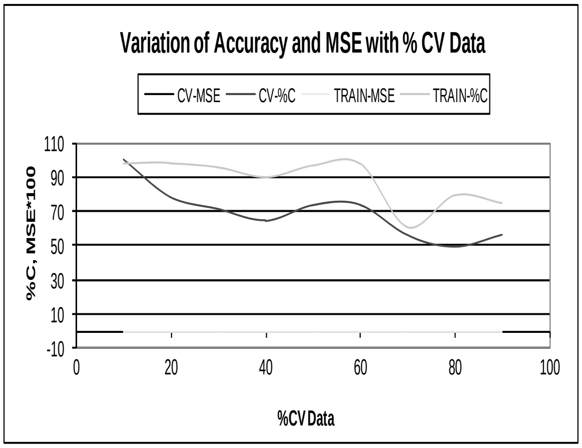


Figure 3. Variation of classification accuracy and MSE with %CV Data

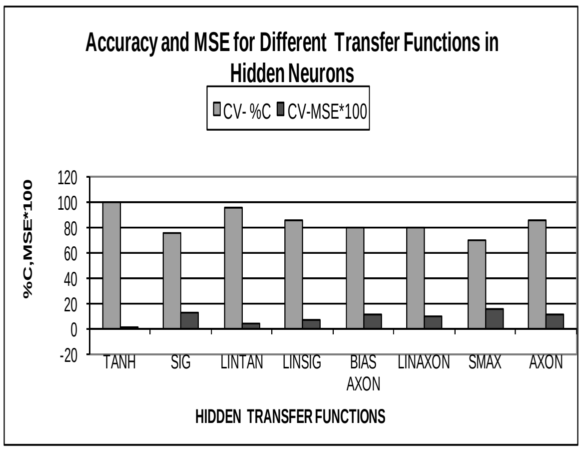


Figure 4. Accuracy and MSE based on different hidden neuron Transfer Functions.

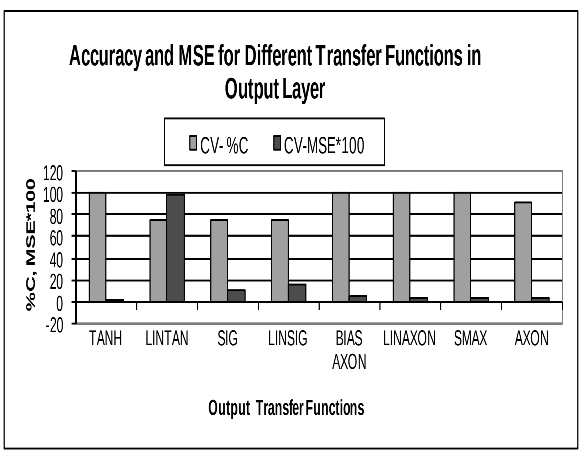


Figure 5. Accuracy and MSE for Output Transfer Function

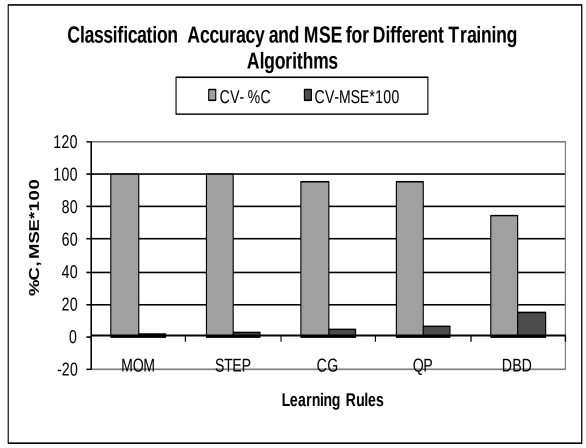


Figure 6. Accuracy and MSE for different Learning Algorithms

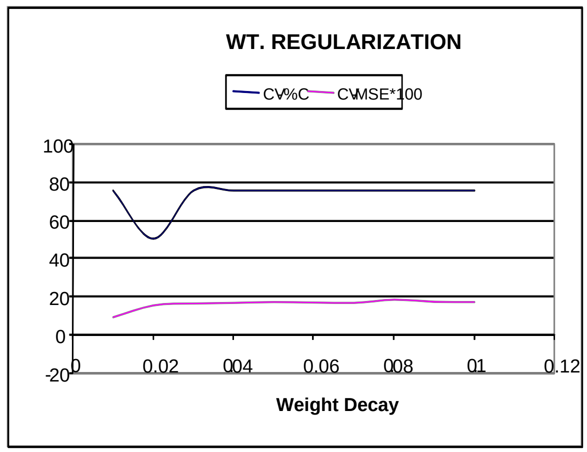


Figure 7. Accuracy and MSE for weight regularization at hidden and output layer

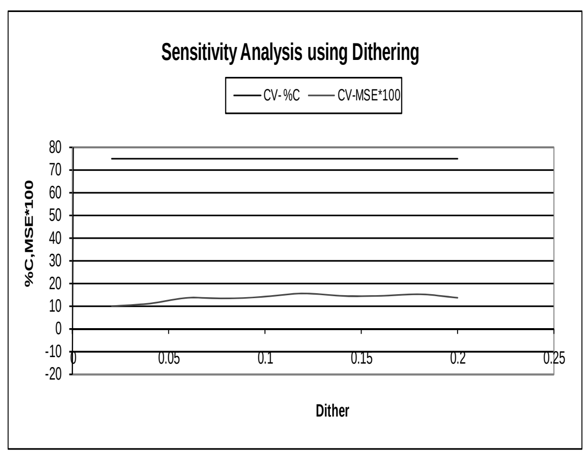


Figure 8. Accuracy and MSE for % input variation

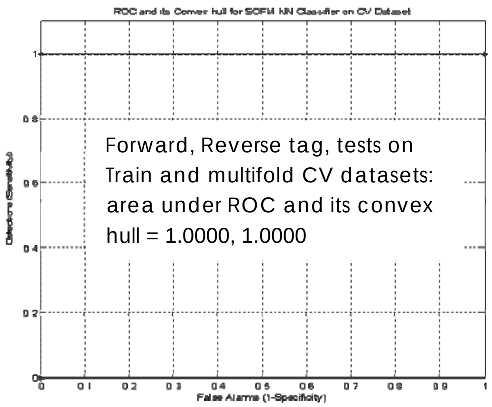


Figure 9. ROC curves for SOFM NN classifier on CV dataset

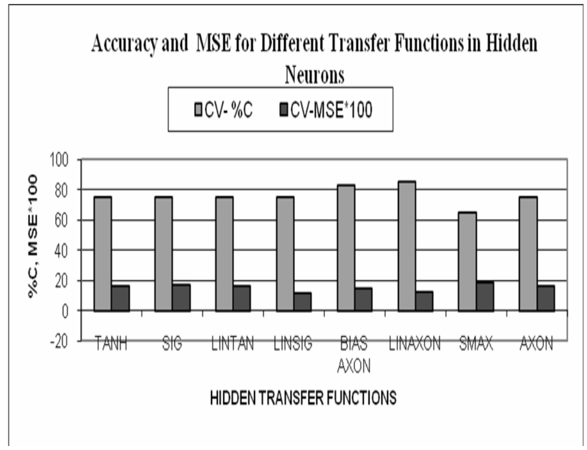


Figure 10. Accuracy and MSE based on different hidden neuron Transfer Functions.

Table 3. Variable Parameters of SOFM

Unsupervised learning rule epochs 100, learning rate starts at 0.01 and decay to 0.001, supervised learning rule epochs 1000 with MSE termination, row 8, column 8, start radius 2, final radius 0, neighborhood shape square Kohonen, dither 0.1, weight 0.01

Parameter	Typical Range	Optimal values
Exemplars for training =N	10% to 90%	90% (56) S=16, D=40
Exemplars for cross validation	10% to 90%	10% (06) S=02, D=04
Number of Epochs	1000 to 10000	1000
Number of hidden layers	1 to 3	1
Number of hidden neurons	2 to 100	34
Transfer function of neurons in hidden layer	Tanh, Sigmoid, Linear Tanh, Linear Sigmoid, Bias axon, Linear axon, Soft Max, Axon	Tanh
Transfer function of neurons in Output layer	Tanh, Sigmoid, Linear tanh, Linear Sigmoid, Bias axon, Linear axon, Soft Max, Axon	Tanh
Supervised Learning Rule	Step, Momentum, Conjugate Gradient (CG), Lavenberg Marquardt, Quick Propagation (QP), Delta bar delta.	Momentum
Momentum rate	0 to 1	0.7
Step Size at hidden and output layer	0 to 1	Hidden: 1.0 Output: 0.1
Weight Regularization at hidden and output layer	0.01 to 0.1 with step 0.01	0.01 without decay
Dither	0.02 to o.2	0.1
Training Time per Epoch per Exemplar per run 0.0811 msec		
Number of free parameters = P (connection weights), N/P Ratio	I*H1 PE's + H1 PE's * Output PE's +(H1+ O/P) PE's	376 0.1489

Table 4. Performance Measures of SOFM NN's Classifier

Data sets	Survival instances		Death instances		ROC Analysis Area under ROC and its convex hull
	Accuracy	MSE	Accuracy	MSE	
8:34:2 SOFM	100	0.0364	83.33	0.0367	0.9077, 0.9127
On 90%train data	100	0.0113	97.90	0.0106	1.0000, 1.0000
On 10%CV data	100	0.0013	100	0.0019	1.0000, 1.0000
Three Fold CV	100	0.0060	95	0.0090	1.0000, 1.0000
6:14:2 SOFM CV	100	0.0150	100	0.0200	1.0000, 1.0000
On train data	100	0.0270	97.5	0.0260	1.0000, 1.0000
Three Fold CV	90	0.0946	100	0.0911	0.9898, 1.0000

3 EXPERIMENTAL DETERMINATION OF NEAR-OPTIMAL JORDAN NN CLASSIFIER

Table 5. Variable Parameters of JORDAN NN

Topology =fourth, Context unit time= 0.1, Transfer function of context unit= Integrator Axon

Parameter	Typical Range	Optimal values
Exemplars for training	10% to 90%	90% (56) S=16, D=40
Exemplars for cross validation	10% to 90%	10% (06) S=02, D=04
Number of Epochs	1000 to 10000	1000
Number of hidden layers	1 to 3	1
Number of hidden neurons	2 to 100	50
Transfer function of neurons in hidden layer	Tanh, Sigmoid, Linear Tanh, Linear Sigmoid, Bias axon, Linear axon, Soft Max, Axon	Linear axon
Transfer function of neurons in Output layer	Tanh, Sigmoid, Linear Tanh, Linear Sigmoid, Bias axon, Linear axon, Soft Max, Axon	Tanh
Supervised Learning Rule	Step, Momentum, Conjugate Gradient (CG), Lavenberg Marquardt, Quick Propagation (QP), Delta bar delta.	Delta bar delta.
Momentum Constant	0 to 1	
Step Size at hidden and output layer (Learning Rate)	0 to 1, Additive 0.01, multiplicative 0.1, smoothing 0.5 at hidden and output	Hidden: 0.1 Output: 0.1
Training Time per Epoch per Exemplar	0.3571 msec	
Number of free parameters, P (connection weights), N/P Ratio	I*H1 PE's + H1 PE's * Output PE's + (H1+ Output) PE's	552 0.1014

Table 6. Performance Measures of JORDAN NN Classifier

Data sets	Survival instances		Death instances		ROC Analysis Area under ROC and its convex hull
	Accuracy	MSE	Accuracy	MSE	
Test on 50% data	50	0.4181	50	0.5585	0.7500, 0.8750
90%train,10%CV On train data	100	0.0030	95	0.0798	1.0000,1.0000
On CV data	100	0.0030	100	0.0025	1.0000,1.0000
Three Fold CV	100	0.092	75	0.079	0.8339,0.8795

Table 7. Comparison of SOFM NN and JORDAN NN Classifier on Different Test Data Sets

Classifier	Data Set	Performance Measures of a classifier on test data set				
		Average Accuracy %	Area under ROC and its convex hull	Training Time per Epoch per Exemplar per run	Complexity N/P Ratio	MSE
SOFM NN 08:34:02	Case 1: Normal tagging order	100	1.0000, 1.0000	0.0811msec	376/56 =0.1489	0.0026
	Case 2: Reverse tagging order	100	1.0000 1.0000			0.0021
SOFM NN 06:14:02	Case 1: Normal tagging order	100	1.0000 1.0000	0.0487 msec	= 0.4375	0.0175
	Case 2: Reverse tagging order	98.75	0.9893, 1.0000			0.0150
JORDAN NN 08:50:02	Case 1: Normal tagging order	100	1.0000, 1.0000	0.3571 msec	552/56 =0.1014	0.0027
	Case 2: Reverse tagging order	87.55	0.8395, 0.8785			0.0112

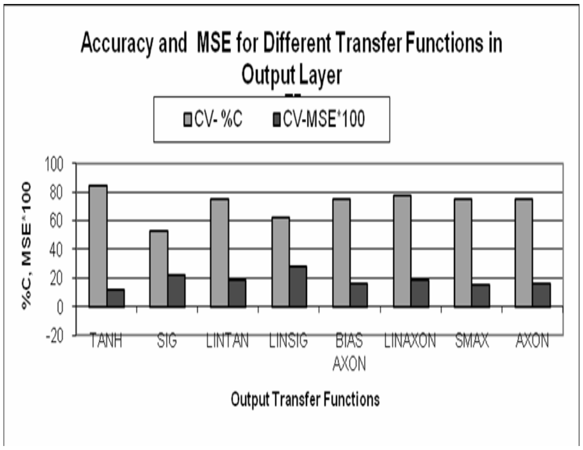


Figure 11. Accuracy and MSE for Output Transfer Function

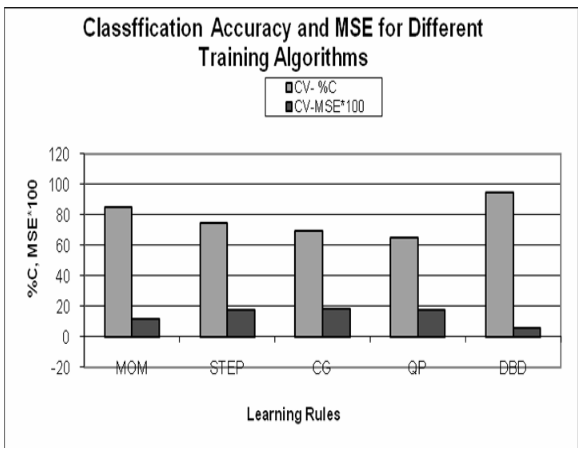


Figure 12. Accuracy and MSE for different Learning Algorithms

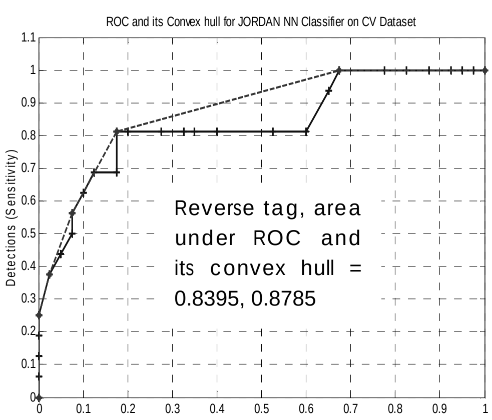


Figure 13. ROC curves for JORDAN NN classifier on CV dataset

Performance evaluation of designed SOFM NN classifier exhibited in Tables 4 to 7 proves that, it satisfies almost all the essential qualities and tests of a near- perfect (near-optimal) classifier up to the end- user's expectations. From Figure 9, ROC Curve of SOFM NN on validation data, it is seen that classifier produces 100% correct detections at 08.2903% false alarms. Thus the specificity of this classifier is calculated as specificity = (1-False Alarms)* 100 and it is 92.7%. The area under ROC Curve comes to about 1.0000 on train test and cross validation. Results of ROC analysis of SOFM NN are giving excellent performance on training and CV dataset when different data partition is used for training and testing. Hence this SOFM NN is able to operate as reasonable classifier [Reyneri L.M.,]. The detection and classification results are shown in Table 4. ROC Curve of JORDAN NN on cross validation data is sketched in Figure 13.

4 DIMENSIONALITY REDUCTION USING PRINCIPAL COMPONENT ANALYSIS

Reduction in dimensionality of input space and hence the network can be achieved by Principal Component Analysis (PCA). PCA is performed using XLSTAT2008. Experimentation is done using Pearson (n), Pearson (n-1), Covariance (n-1), Covariance (n), Spearman, Kendall and Polychonic types, out of which Pearson (n) rule is found best. Figure 14 displays eigenvalues and Figure 15 demonstrates variation of average classification accuracy on number of principal components as inputs. It reflects the quality of the projection from 8 to 6 dimensions. Using the factors of PCA, by similar experimentations, optimal SOFM NN is designed with following parameters.

Inputs = 06, Number of hidden neurons =14, Transfer function of neurons in hidden and output layer = Tanh, Unsupervised learning rule epochs 100, learning rate starts at 0.01 and decay to 0.001, supervised learning rule epochs 1000 with MSE termination, Learning rule = Momentum, row 3, column 3, start radius 2, final radius 0, neighborhood shape square Kohonen, dither 0.1, weight 0.01. Number of connection weights reduced to 128 and this network converges fast within 0.0487 msec. Training and testing results are compared.

5 RESULTS AND DISCUSSION

The possible parameter variations chosen for this JORDAN NN are depicted in the Table 5 and performance in Table 6. Table 7 exhibits comparison of performances between SOFM NN, dimensionally reduced SOFM NN and JORDAN NN. It is evident that SOFM NNs is giving consistent accuracy over all datasets. ROC analysis is perfect, approaching unity. This simplicity and compactness in the structure indicates the feasibility of the SOFM NN for the online implementation, and the hardware implementation. It also implies that the SOFM NN as a classifier for this work possesses more learning ability than the corresponding JORDAN NN. As per the confusion matrices it was found that the SOFM neural classifier has the advantage of reducing misclassifications among the neighborhood classes compared to JORDAN NN classifier. It provided consistent classification accuracy over 10 runs for both, survival and death instances. We achieved 100% classification accuracy over both of training and cross validation (unseen data sets) and the system runs in a 0.0487 millisecond in the environment of Intel Pentium 4 PC with 2.4 GHz CPU and 1 GB DDRAM.

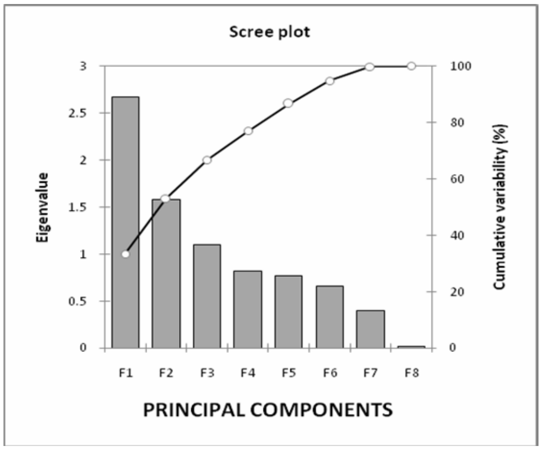


Figure 14. Principal Components, Eigenvalues and Cumulative Variability from PCA

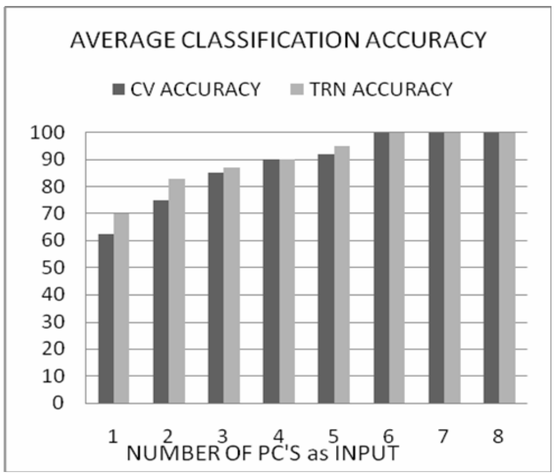


Figure 15. Variation of Accuracy with number of Principal Components

6 CONCLUSION

The study group included 18 survivors and 44 death patients' cases. This study confirms that SOFM NN artificial neural networks out performs JORDAN NN and can offer a useful approach for developing diagnostic algorithms for chest pain patients. It is observed that SOFM is fastest network, simple in design and synthesis, lowest average MSE, highest accuracy and ROC analysis is perfect approaching unity. Significant (65.96 %) reduction in connection weights is achieved with PCA. These issues have not been addressed in previous studies. The dimensionally reduced SOFM neural network method has proved to be reliable for implementing quantitative prognosis of mortality in patients with heart failure. Additional studies with larger numbers of patients are required to better assess the usefulness of artificial neural networks [Raut R. D. and Dudul S. V.].

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