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BIOMEDICAL MODELING

Overview of artificial neural network models in the biomedical domain

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ABSTRACT

AIM: The aim of this paper is to provide an overview of artificial neural network (ANN) in biomedical domain and compare it with the logistic regression model.

METHODS: Artificial neural network models and logistic regression models were created and compared using a sample of a modified dataset adapted to the dataset from Framingham Heart Study. R statistical software package is used to create and compare the models.

RESULTS: The results indicated that the ANN model is more accurate in classifying the dependent variable than the logistic regression model (84.4 % vs 82.9 %).

CONCLUSION: This paper has shown the effect of artificial neural network models in classifying the survival status (event or non-event) *(Tab. 2, Fig. 4, Ref. 29)*. Text in PDF *www.elis.sk.*

KEY WORDS: artificial neural network, prediction, classification, logistics, biomedical.

Introduction

Artificial neural network (ANN) models are gaining importance in the field of the predictive modelling because of its capabilities of modelling nonlinear relationships in a high-dimensional dataset. Artificial neural network models are able to predict a complex relationship between variables, which is not otherwise possible with other models such as logistic regression models. Artificial neural network models are used in different fields such as image processing, clinical diagnosis (especially that of cancer): fraud detection in financial sector, and weather forecasting.

Concepts and types of artificial neural network

Artificial neural network models work on the principles of biological neural network (1) where each neuron is connected with other neurons. It has two parts, namely the dendrites and the axon. The dendrites act as receivers and the axon acts as the transmitter of information. The nucleus of the neuron contains the information that is to be transferred.

Artificial neural networks consist of an input layer, hidden layers and output layer while the information is fed into the model through the input layer, processed through the hidden layers and put out from the output layer (Fig. 1).

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1) Basic definition and concepts in artificial neural networks

Activation function

Activation function is used to transfer the weighted sum of inputs into the output.

i. Sigmoidal function

Sigmoidal function (2) is an 'S' shaped function which was used in modelling the nonlinear relationships. The sigmoidal function always transforms the input into a range from 0 to 1. This helps us to classify or differentiate the input in terms of distinct categories. The sigmoidal function suffers from the vanishing gradient problem i.e. when the gradient of error during the learning process is very small, the weight is not going to change and thus, there will be no improvement in the prediction.

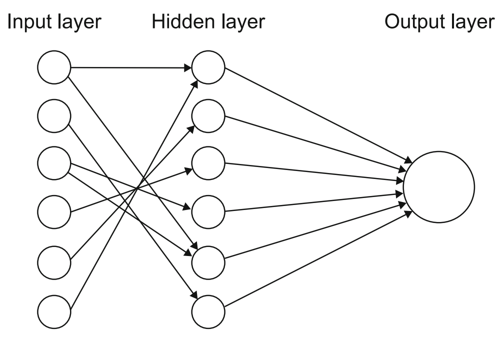

Fig. 1. Neural network structure.

ii. Radial basis function
Radial basis function (3) constructs the distance from the centre. In case of neural networks, the radial basis function compares each input vector against the selected vector (the vector is selected to act as a representative vector among the input vectors). The output value is 1 if the given vector is the selected vector, otherwise it is 0.

iii. Tan-h function
Tan-h function (4) output values are in the range from -1 to 1. Tan-h function also suffers from the vanishing gradient problem.

iv. Rectified linear units
The rectified linear unit (5) function calculates the maximum between the input value and 0. If the input value is less than 0, the output is 0, otherwise it bas the input value. Currently, this is the most widely used activation function in the neural networks as it overcomes the vanishing gradient problems of other activation functions such as sigmoid or Tan-h function.

Exclusive OR (XOR)

Exclusive OR condition provides the status of decision in the exclusive form only (either of the two states, not both).

2) Types of artificial neural networks

The following are the types of neural network models generally used in predicting the relationships.

a) Feedforward artificial neural networks

This is the simplest form of ANNs wherein information flows only in one direction, i.e. from the input to the output layer. The network does not provide any feedback to the input layer.

i. Multi-layer perceptron (MLP)
Multi-layer perceptron (MLP) (2) is one of the feedforward networks where the input values are multiplied with their corresponding weights and fed into the hidden layer while the hidden layer process transfers the weighted input to the output layer with values of multiplied weights corresponding to the output layer (6). MLP uses the backpropagation algorithm to find the weights (7). It uses sigmoidal or threshold function as the activation function.

ii. Radial basis function network (RBFNN)
Radial basis function network (3, 8) is one of feedforward types of network using radial basis function as the activation function

iii. Probabilistic neural network (PNN)

Probability distribution of each data input is determined using Gaussian window function (Gaussian distribution with given standard deviation σ) while Parzen probability distribution function and k classes are created based on the estimated probability. For the input data, the probabilities of k classes are calculated again and the new data input belongs to the k^{th} class if it is greater than the other classes.

b) Feedback artificial neural networks

In feedback networks, the information can travel in two directions, thus creating a loop while transferring the information between input and output layers. The feedback is provided at both layer levels, i.e. at the hidden layer as well as at output layer. The process is completed when the processed information reaches the optimum level. Recurrent neural network is one of the feedback neural networks.

c) Learning vector quantization neural network (LVQNN).
Learning vector quantization neural network converts the given input layer into prototype vectors. New input data which are converted into vectors, compared with prototype vectors using similarity and distance measures and assigned to the closest prototype vector.

3) Application of artificial network in biomedical domain

Due to their ability to analyse the data with nonlinear relationship, ANN models are being extensively used in the area of diagnosis (9, 10, 11): prognosis (12): classification (13): prediction (14, 15, 16, 17): and survival analysis (18).

Neural network models are used in processing images (19, 20) in radiology, nuclear medicine, dermatology and pathology.

ANN models are applied to interpret and classify the signals from electroencephalogram (EEG) and electrocardiogram (ECG).

4) Comparison with traditional statistical models

Table 1 compares the artificial neural network models and traditional models such as logistic regression models (21, 22, 23, 24, 25)

Methods

Example of artificial neural network using R Statistical Package

The following example uses R open source statistical computing software (26) which is useful for carrying out various statistical tests and methods, graphics, text and data mining procedures (27). The data set used in the example is adapted to the dataset from the Framingham heart study (28) used in their book titled "Statistical Modeling for Biomedical Researchers" (29) and the dataset is modified for illustrative purposes to suit the objective of the study. The results are shown for illustrative purpose only, as they are not meant to represent the true performance of the ANN model.

Tab. 1. Comparison between ANN and traditional statistical models.

Parameters	Artificial neural network
Ability to analyse nonlinear relations	Higher than that in the traditional statistical models
Ability to handle correlated independent variables	Higher than that in the traditional statistical models
Classification accuracy	Higher than that in the traditional statistical models
Interpretation of coefficients/weights	More difficult than that in traditional statistical models
Chances of overfitting	Higher than those in the traditional statistical models

The following steps describe the use of R codes in building the ANN models using the dataset and compare it with the logistic regression model

Step 1: Installing required packages
The following packages need to be downloaded and installed in the R environment using the following codes:
install.packages ("neuralnet")
install.packaages ("ROCR")
Step 2: Reading the main data (in csv file format)
maindata<-read.csv („main.csv",header=F)
Step 3: Normalizing the main data file using min and max functions to make all the variables uniform in measurement
normalize = function (x){ (x - min (x))/ (max (x) - min (x))}
maindata.normalized = apply (maindata, 2, normalize)
Step 4: Building the artificial neural network model using neural net package where V16 is the categorical dependent variable (event or non-event) and V2,V3,V9,V10,V11,V12,V14 and V15 are independent variables
library (neuralnet)
nnet<- neuralnet (V16 ~ V2 + V3 + V9 + V10 + V11 + V12 + V14 + V15, data=maindata.normalized, hidden=5, linear.output=FALSE, threshold=0.01)
nnet$result.matrix
Step 5: Plotting the artificial neural network model
plot (nnet) (Fig. 2).
Step 6: Model needs to be created for test data while data without the outcome variable, i.e V16 are to be used.
testdata<-read.csv („ftest1.csv",header=F)
testdata<-testdata (, (c („V2","V3","V9","V10","V11","V12","V14","V15")))
testdata.normalized<-apply (testdata, 2, normalize)
nnet.test <- compute (nnet, testdata.normalized)
testouput<-nnet.test$nnet.result

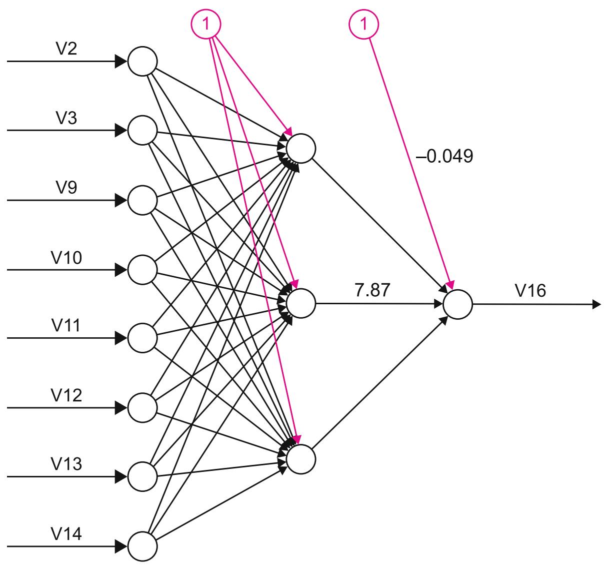

Fig. 2. Neural network model.

Tab. 2. Actual vs prediction.

	Prediction	
Actual	0	1
0	4	34
1	8	171

Step 7: Model built on test data needs to be compared with original data to find out the accuracy of the model. Test data with outcome variable, i.e V16 are to be used.
testdataorignal<-read.csv („ftest.csv",header=F)
testdataoriginal<-testdata2 (, (c („V2","V3","V9","V10","V11","V12","V14","V15","V16")))
predicted<- (min (mydata (, ‚V16')) + testouput * (max (maindata (, ‚V16'))-min (maindata (, ‚V16'))))
Step 8: Compare actual and test data
compareresults <- data.frame (original = testdata2$V16, prediction = predicted)
compareresults
Step 9: Create actual vs prediction table
roundedcompare<-sapply (compareresults,round,digits=0)
roundedcompare=data.frame (roundedcompare)
attach (roundedcompare)
table (orginal,prediction)

The proportion values derived from Table 2 are as follows: true negative is 2 % false negative is 15.6 %, true positive is 78 %, and classification accuracy is found to be 84.4 %

Step 10 Create ROC curve i.e. sensitivity vs 1-specificity
library (ROCR)
roc.prediction = prediction (nnet.result, testdata2$V16)
roccurve <- performance (nn.pred, „tpr", „fpr")
plot (roccurve) (Fig. 3).
Step 11: Building the logistic regression using glm function
logit <- glm (V16 ~ V2 + V3 + V9 + V10 + V11 + V12 + V14 + V15, data=mydata, family = „binomial")

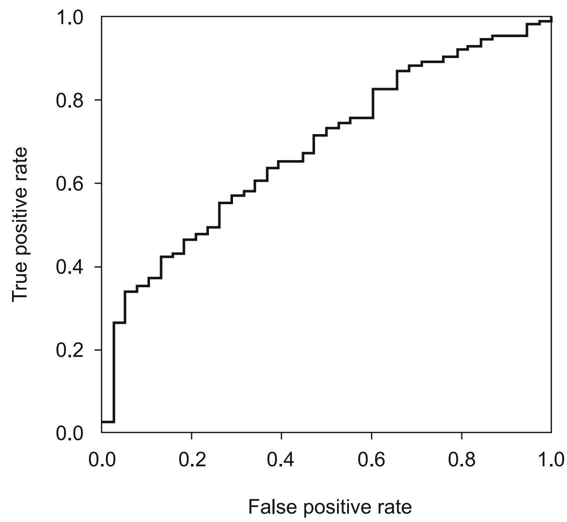

Fig. 3. ROC curve of neural network model.

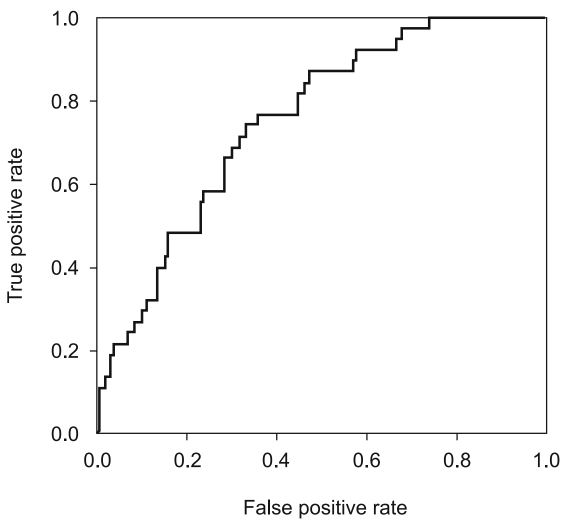

Fig. 4. ROC curve for logistics regression model.

Step 12: Prediction using test data
ftestlogit<-read.csv („ftestlogit.csv",header=F)
test.results <- predict (logit,data1=subset (ftestlogit,select=c („V2 ","V3","V9","V10","V11","V12","V14","V15","V16")): type='response')
test.results <- ifelse (test.results > 0.5,1,0)
Step 13: Classification of model's accuracy
error <- mean (test.results != ftestlogit$V16)
accuracy <- 1-error
The accuracy of the logistic regression model was found out to be 82.9 % which is less than that of the ANN model (84.6 %)
Step 14: Create ROC curve, i.e. sensitivity vs 1-specificity
library (ROCR)
Logitpred <- prediction (test.results, ftestlogit$V16)
logitpr <- performance (logitpred, „tpr", „fpr")
plot (logitpr) (Fig. 4).

Results and discussion

Figure 2 provides the neural network model with 8 input variables, hidden layers and one output variable. Table 2 provides the comparison between actual and predicted values using the neural network. The Table 2 indicates that the true negative is 2 %, false negative is 15.6 %, true positive is (78 %): and classification accuracy is found to be 84.4 %. The classification accuracy of the logistics regression model is obtained from Step 13, which is 82.9 %.

Results indicated that the ANN model is more accurate in classifying the dependent variable than the logistic regression model (84.4 % vs 82.9 %). When comparing the above two models and ROC curve, the ANN model is found to be more accurate in classifying the dependent variable under study. One of the limitations of ANN models lies in the interpretation of weights while the predictors of ANN models are not as easy as those in other traditional statistical models.

Conclusion

The paper provides an overview of artificial neural network by specifying its types and application in biomedical domain. It illustrates the method of building the ANN model using the R statistical package and provides an example. It also compared the ANN model with the logistic regression model while the results indicate that the ANN model is more accurate in classifying the dependent variable than the logistic regression model.

References

1. **Eluyode OS, Akomolafe DT.** Comparative study of biological and artificial neural networks. Eur J Appl Engin Sci Res 2013; 2 (1): 36–46.

2. **Hornik K, Stinchcombe M, White H.** Multilayer feedforward networks are universal approximators. Neural Networks 1989; 2 (5): 359–366.

3. **Mehrazin A, Taghipour M, Froutan O, Ghabdian B, Soleimani H.** Radial basis function in artificial neural network for prediction of bankruptcy. Internat Business Res 2013; 6 (8): 121.

4. **Fan E.** Extended tanh-function method and its applications to nonlinear equations. Phys Lett 2000; 277 (4): 212–218.

5. **Dahl GE, Sainath TN, Hinton GE.** Improving deep neural networks for LVCSR using rectified linear units and dropout. In Acoustics, Speech and Signal Processing (ICASSP): 2013 IEEE International Conference on (8609–8613).

6. **Welch RL, Ruffing SM, Venayagamoorthy GK.** Comparison of feedforward and feedback neural network architectures for short term wind speed prediction. Neural Networks, 2009. IJCNN 2009. International Joint Conference on (3335–3340).

7. **Jain AK, Mao J, Mohiuddin KM.** Artificial neural networks: A tutorial. Computer 1996; 29 (3): 31–44.

8. **Musavi MT, Ahmed W, Chan KH, Faris KB, Hummels DM.** On the training of radial basis function classifiers. Neural Networks 1992; 5 (4): 595–603.

9. **Amato F, López A, Peña-Méndez EM, Vaňhara P, Hampl A, Havel J.** Artificial neural networks in medical diagnosis. 2013.

10. **Sandhu IK, Nair M, Shukla H, Sandhu S.** Artificial neural network: As emerging diagnostic tool for breast cancer. Internat J Pharm Biol Sci 2015; 5 (3): 29–41.

11. **Moein S.** (Ed.). Medical diagnosis using artificial neural networks. IGI Global. 2014.

12. **Walczak S, Velanovich V.** Improving prognosis and reducing decision regret for pancreatic cancer treatment using artificial neural networks. Decision Support Systems 2018; 106: 110–118.

13. **Esteva A, Kuprel B, Novoa RA, Ko J, Swetter SM, Blau HM, Thrun S.** Dermatologist-level classification of skin cancer with deep neural networks. Nature 2017; 542 (7639): 115.

14. **Ho-Le TP, Center JR, Eisman JA, Nguyen TV, Nguyen, HT.** Prediction of hip fracture in post-menopausal women using artificial neural network approach. In Engineering in Medicine and Biology Society (EMBC): 2017 39th Annual International Conference of the IEEE (4207–4210).

15. **Fei Y, Hu J, Li WQ, Wang W, Zong GQ.** Artificial neural networks predict the incidence of portosplenomesenteric venous thrombosis in patients with acute pancreatitis. J Thromb Haemost 2017; 15 (3): 439–445.

16. Rau HH, Hsu CY, Lin YA, Atique S, Fuad A, Wei LM, Hsu MH. Development of a web-based liver cancer prediction model for type II diabetes patients by using an artificial neural network. Computer Method Program Biomed 2016; 125: 58–65.

17. Li H, Luo M, Zheng J, Luo J, Zeng R, Feng N et al. An artificial neural network prediction model of congenital heart disease based on risk factors: A hospital-based case-control study. Medicine 2017; 96 (6).

18. Averitt AJ, Natarajan K. Going Deep: The Role of Neural Networks for Renal Survival and Beyond. 2018.

19. Kahn Jr CE. From Images to Actions: Opportunities for Artificial Intelligence in Radiology. 2017.

20. Waal I. Skin cancer diagnosed using artificial intelligence on clinical images. Oral diseases. 2017.

21. Faradmal J, Soltanian AR, Roshanaei G, Khodabakhshi R, Kasaeian A. Comparison of the performance of log-logistic regression and artificial neural networks for predicting breast cancer relapse. Asian Pac J Cancer Prev 2014; 15 (14): 5883–5888.

22. Tu JV. Advantages and disadvantages of using artificial neural networks versus logistic regression for predicting medical outcomes. J Clin Epidemiol 1996; 49 (11): 1225–1231.

23. Eftekhar B, Mohammad K, Ardebili HE, Ghodsi M, Ketabchi E. Comparison of artificial neural network and logistic regression models for prediction of mortality in head trauma based on initial clinical data. BMC Med Inform Decis Making 2005; 5 (1): 3.

24. Kurt I, Ture M, Kurum AT. Comparing performances of logistic regression, classification and regression tree, and neural networks for predicting coronary artery disease. Expert System Appl 2008; 34 (1): 366–374.

25. Ayer T, Chhatwal J, Alagoz O, Kahn Jr CE, Woods RW, Burnside ES. Comparison of logistic regression and artificial neural network models in breast cancer risk estimation. Radiographics 2010; 30 (1): 13–22.

26. https://cran.r-project.org/

27. Renganathan V. Tutorial on mining of biomedical literature with the help of R Package. http://www.vinaitheerthan.com 2 (1). 1–7

28. https://biolincc.nhlbi.nih.gov/studies/fhs/

29. Dupont WD, Dupont WD. Statistical modeling for biomedical researchers: a simple introduction to the analysis of complex data. Cambridge University Press. 2009.

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