ARTIFICIAL NEURAL NETWORKS IN BIOMEDICAL ENGINEERING: A REVIEW

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ABSTRACT
This paper presents a review of applications of artificial neural networks in biomedical engineering area. Artificial neural networks in general are explained; some limitations and some proven benefits of neural networks are discussed. Use of artificial neural network techniques in various biomedical engineering applications is summarised. A case study is used to demonstrate the efficacy of artificial neural networks in this area. The paper concludes with a discussion of future usage of artificial neural networks in the area of biomedical engineering.

KEYWORDS
Artificial neural network, Biomedical engineering, Breast cancer, k-fold cross-validation

1. INTRODUCTION

Artificial neural networks (ANNs), the branch of artificial intelligence, date back to the 1940s, when McCulloch and Pitts developed the first neural model. Since then the wide interest in artificial neural networks, both among researchers and in areas of various applications, has resulted in more-powerful networks, better training algorithms and improved hardware. The basic problem solved by ANNs is the inductive acquisition of concepts from examples. The ability to learn and generalize from data, that is to mimic the human capability to learn from experience, makes ANNs useful in automating the process of learning rules from various applications.

Biomedical Engineering is an interdisciplinary domain, which links many disciplines such as engineering, medicine, biology, physics, psychology, etc (Wolff 1970). This rapidly growing field must meet the needs of industrial, clinical, and scientific research communities. It involves the application of state-of-the-art technology to the creation of methodologies and devices for human welfare and for better understanding of human biological processes. Artificial neural network is one of the techniques that can be utilised in these applications. This paper explores the possibilities of applying ANNs in biomedical engineering area.

The goal of this paper is to review the current issues in biomedical engineering being addressed using artificial neural network methods. The next section explains artificial neural networks in general, their rule learning process, their applications and the need for using them in biomedical engineering domain. Section 3 reviews some of the biomedical engineering applications that have utilised artificial neural network methods. Section 4 demonstrates the efficacy of utilising neural network methods in biomedical engineering domain by analysing a breast cancer database. Finally the paper is concluded with some future suggestions.

2. INTRODUCTION TO ARTIFICIAL NEURAL NETWORKS

Artificial neural networks have been extremely valuable for learning from examples and making predictions for unseen examples. ANNs have been successfully applied to a wide range of pattern recognition and function approximation problems, (Mitchell 1997). Consequently the field has generated interest from researchers in such diverse areas as engineering, medicine, computer science, psychology, neuroscience, physics, and mathematics, (Murray 1992).

2.1 What is a Neural Network?

ANNs are a powerful general-purpose tool applied to many tasks where data relationships have to be learned or, decision process and predictions have to be modelled from examples. ANN methods determine the procedure for correctly predicting new unseen examples, if given the description of a set of examples (Browne 1997).

ANNs represent the computational paradigm that is based on the way biological nervous systems, such as the brain, process information. An ANN is a parallel distributed information processing structure consisting of processing elements interconnected via unidirectional signal channels called links.

An ANN consists of one or more layers of nodes configured in regular and highly connected topologies. The commonest type of ANN consists of three layers: an input layer (consists of input nodes), an output layer (consists of output nodes) and a hidden layer (consists of hidden nodes). Raw information is fed into the network via input nodes. The activities of input nodes along with the weights on links between input and hidden nodes determine outputs of hidden nodes. Behaviour of the output nodes depends on the activities of hidden nodes and the weights on links between hidden and output nodes.

A feedforward network allows signals to move from input to output nodes only. There is no feedback from output to input/hidden nodes or lateral connections among the same layer. A feedback network allows signals to travel in both directions by introducing loops in the network. For example in the recurrent model, outputs from hidden nodes feed back to some of the input nodes.

There are single-layer and multi-layer architectures. In single layer architectures, for example the Hopfield model (Browne 1997), a single layer of nodes forms the topology. The output from each node feed back to all of its neighbours. Whereas in multi layer architectures, several layers of nodes form the topology.

Neural networks have capability of transforming inputs into desired output changes; this is called neural network learning or training. These changes are generally produced by sequentially applying input values to the network while adjusting network weights. This is similar to learning in biological systems that involve adjustments to the synaptic connections that exist between the neurones. During the learning process, the network weights converge to values such that each input vector produces the desired output vector.

There are three major categories of learning: (1) supervised in which the network is provided the expected output and trained to respond correctly (2) unsupervised in which the network is provided with no knowledge beforehand of expected output and trained to discover structures in presented inputs (3) reinforcement in which the network is not provided with explicit output instead it is periodically given performance indicators.

2.2 Why use Neural Networks?
Applications in biomedical engineering area often involve analysis and classification of an experiment's outcomes. This can be obtained using traditional techniques such as linear discriminant function and the analysis of covariance. But in some cases, outcome of experiments is dependent on a number of variables, with the dependence usually an unknown nonlinear function. Neural networks can manage such problems. ANN bridges the much needed gap between technical knowledge and biology. Investigation of ANN methods in biomedical engineering domain will advance medical care.

2.3 Rule extraction from artificial neural networks
A recognised shortcoming of ANNs is the inability to explain the decision process in a comprehensive form by which a trained network arrives at a specific conclusion. Understanding a trained neural network is desirable for many reasons. For a medical diagnosis, airline or power station security system, it is important that the system's user should be able to validate output of the trained ANN under all possible input conditions.

The decision process of a trained network can be interpreted by translating the stored knowledge (connection weights) into symbolic rules. Rule extraction from ANNs can help to explain their behaviour and also facilitates the transfer of learning (from ANNs to expert system by automating the knowledge bases). The exercise of rule-extraction from ANNs is important due to: (1) in real life situations, systems that declare the learned knowledge explicitly are adopted more freely (such as symbolic machine learning systems); (2) the rule base generated from the trained ANN is sometimes sufficient for accurate modelling of the given domain; and (3) in some cases the ability to explain how a solution is arrived at is essential in practical systems (for example controlling power regulation in a power system) (Nayak 2000). Due to these reasons, rule extraction is particularly important for biomedical engineering domains.

2.4 Typical Applications
ANNs are a powerful general purpose tools applied to many machine learning tasks. The ANN learning method provides a robust and non-linear approach to approximating the target function for classification (discrete valued), regression (continuous valued) and clustering problems.

Since neural networks are best at identifying patterns or trends in data, they are well suited for prediction or forecasting including sales forecasting, industrial process control, customer research, data validation, risk management and target marketing. ANNs have been successfully applied to many other practical problems such as interpretation of complex real world remote sensing data, recognition of handwritten characters, spoken words, and faces, forecasting of an economical generating schedule for a power system, modelling complex environmental data, force predictions in mills, machine intelligence in a mass transit railway system and self calibration of a space robot (McCulloch & Pitts 1943, Mitchell 1997, Nayak 2000).

3. APPLICATIONS OF ANN IN BIOMEDICAL ENGINEERING DOMAIN

Artificial Neural Networks are currently a 'hot' research area in medicine and it is believed that they will receive extensive application to biomedical systems in the next few years. At the moment, the research is mostly on modelling parts of the human body and recognising diseases from various scans (e.g. cardiograms, CAT scans, ultrasonic scans, etc.) (Christos & Dimitrios 1996).

Table 1 below demonstrates that neural networks are ideal in recognising diseases using scans since there is no need to provide a specific algorithm on how to identify the disease. Neural networks learn by example so the details of how to recognise the disease are not needed. What is needed is a set of examples that are representative of all the variations of the disease. The quantity of examples is not as important as the 'quality'. The examples need to be selected very carefully if the system is to perform reliably and efficiently (Christos & Dimitrios 1996).

TABLE 1
NEURAL NETWORKS IN BIOMEDICAL APPLICATIONS

Types Of Neural Networks	Application
ARTMAP	Cancer (Downs et. al 1998)
	ECG (Suzuki 1995)
Bayesian	EMG (Cheng et. al 1992)
Feedforward, Backpropagation	Cancer (Ohno-Machado& Bialek 1998, Theeuwen et.al 1995)
	Cardiovascular System (Keller et. al 1995)
	ECG (Hu et. al 1992)
	Electromyogram (Hassoun et. al 1992)
	Human Gait Analysis (Rodrigues et. al 1999)
	Medical Image Analysis (Karkanis et. al 2000)
	Prescriptions/Drugs (Bryne et. al 2000)
Hopfield	Medical Image Analysis (Tsai et. al 1998)
Neuro-Fuzzy	Simulation of Elastic Tissue (Radetzky et. al 1998)
Resilient Propagation	Medical Image Analysis (Lasch et. al 2000)

4. A CASE STUDY: BREAST CANCER PROBLEM DOMAIN

To demonstrate the effectiveness of neural networks in biomedical engineering domain, we carry on ANN experiments on breast cancer database. This database contains instances of various breast cancers in several patients. The target of the Breast Cancer database is to distinguish between the benign and malignant type of cancer according to nine attributes such as Clump thickness, Cell size, Cell shape, Adhesion, Bare nuclei, Nucleoli, etc. The data set has 699 instances from which 16 instances were removed due to missing information about the Single epithelial cell size attribute. All the eliminated 16 patterns were instances of benign type that already has a major distribution in instance space. The resulting database contains 683 attributes, 444 of them are of benign type and the remaining 239 are of malignant type of cancer.

To reduce learning complexity in neural networks and assist in understanding the dependencies among attributes and target concepts, we discretise (categorise) attributes and use the sparse-coding representation. Each value of a discrete attribute with *n* possible values is represented by an *n*-bit binary string, with only one bit carrying a value of one corresponding to the attribute's value. For example, *cell size* is a feature that has three values *small, medium, large*. This will be converted into three binary features as *size_small, size_medium, and size_large* representing the sparse-coding of {1 0 0}, {0 1 0}, and {0 0 1} respectively. This type of coding resulted in the input layer with 90 nodes.

To avoid the initial guess of neural network architecture, we use the cascade correlation algorithm one of the methods for incrementally building a feedforward network that starts with an input and an output layer with no hidden units. This algorithm constructs the network by initially training a two layer (input and output nodes) model only, and then gradually adding hidden nodes until an acceptable overall network is achieved. The goal is to develop a small size feedforward ANN with sigmoidal nodes that properly classifies the training and unseen examples. The Breast Cancer problem domain utilizes a 5-fold CV scheme to produce the ANN solutions. The best network obtained has a size of 90 input nodes, 2 hidden nodes and 1 output nodes.

Training of the neural network on this database means that the resulting model should be able to diagnose an individual. The resulting model must mimic the relationship among physiological variables (such as Clump thickness, Cell size, Cell shape, Adhesion, Bare nuclei, Nucleoli, etc, that we have used for training) even at different physical activity levels. If a model is adapted to an individual (pattern used for testing the network), then it should be able to correctly predicting the medical condition of that individual.

When training of the network has ceased, the root mean square error (RMSE) is reduced to 0.0054. The trained network was able to completely recognise the benign and malignant types of cancer. From the patterns that were used for training, a 100% accurate classification was achieved. While generalising with the unseen patterns, the RMSE was 0.1887 (when tested on 239 unseen individuals, only 7 of them were incorrectly predicted), thus yielding a high accuracy of the trained network.

This small experiment shows that the neural networks trained on the breast-cancer problem database were capable of predicting the new unseen cases with a high accuracy. This demonstrates that neural networks can be successfully applicable to biomedical engineering domain.

5. CONCLUSION AND FURTHER STUDY

It is obvious from our study that neural networks have been used successfully in many areas in biomedical engineering. It is obvious from literature that researchers have used neural networks as computational tools, modeling tools as well as human brain mimicking tool. Some potential biomedical engineering fields where neural networks can be applied in future are electrophysiology, biomaterials, biotechnology, biosensors, modelling, instrumentation, rehab engineering, medical analysis, prothetic, informatics, imaging, clinician, biomechanics, computers devices.

REFERENCES

1. Browne A. (1997). *Neural Network Analysis, Architectures, and Applications*, Philadelphia : Institute of Physics.
2. Byrne S., Cunningham P., Barry A., Graham I., Delaney T. and Corrigan O.I. (2000). Using Neural Nets for Decision Support in Prescription and Outcome Prediction in Anticoagulation Drug Therapy. http://ai.ijs.si/Branax/idamap-2000_AcceptedPapers/Byrne.pdf
3. Cheng K.S., Chan D.Y., and Liou S.H. (1992). A Subband Coding Scheme and the Bayesian Neural Network for EMG Function Analysis. *International Joint Conference on Neural Network.* **II-**931-934.
4. Christos S. and Dimitrios S. (1996) Neural Networks. http://www.doc.ic.ac.uk/~nd/surprise_96/journal/vol4/cs11/report.html

5. Downs J., Harrison R.F., and Cross S.S. (1998). A Decision Support To ol for the Diagnosis of Breast Cancer Based Upon Fuzzy ARTMAP. *Neural Computing & Applications* **Vol 7 No 2** , 147-165.
6. Hassoun M.H., Wang C., and Spitzer A.R. (1992). Electromyogram Decompositi on via Unsupervised Dynamic Multi-layer Neural Network. *International Joint Conference on Neural Network.* **II-**405-411.
7. Hu Y.H., Tompkins W.J., and Xue Q. (1992). Artificial Neural Network for ECG Arrhythmia Monitoring. *International Joint Conference on Neural Network.* **II-**987-991.
8. Karkanis S., Magoulas G.D. and Theofanous N. (2000). Image Recognition and Neuronal Networks: Intelligent Systems for the Improvement of Imaging Information. *Minimal Invasive Therapy and Allied Technologies.* **August 2000 Vol. 9, N o. 3 -4,** 225-230**.** http://www.brunel.ac.uk /csstgdm mitat.pdf
9. Keller P.E., Kangas L.J., Hashem S., Kouzes R.T. and Allen P.A (1995). A Novel Approach to Modelling and Diagnosing the Cardiovascular Sy stem. *World Congress on Neural Networks (WCNN'95).* **Washington DC July 17 -21 1995.** http://www.emsl.pnl.gov:2080/proj/neuron/papers keller.wcnn95.pdf
10. Lasch P., Lewis E.N., Kidder L.H and Naumann D. (2000). Image Reconstruction of FT-IR Micro-spectrometric Data. http://midas.rki.de/publications/SPIE_LEW.pdf
11. McCulloch W., and Pitts W. (1943). A logical calculus of the ideas imminent in nervous activity. *Bulletin of Mathematical Biophysics* **5:** 115-33.
12. Mitchell T. (1997). *Machine Learning*. The McGraw-Hill Companies, Inc.
13. Murray A.F. (1992). *Applications of Neural Networks,* Cambridge Tracts in Theoretical Computer Science (30), Cambridge University Press.
14. Nayak R. (2000). Gyan: A Methodology for Rule Extraction From Neural Networks. *Ph.D. Thesis, Queensland University of Technology*, *2000*. www.cis.unisa.edu.au/~cisrn/thesis.ps
15. Ohno-Machado L. and Bialek D. (1998). Diagnosing Breast Cancer fr om FNAs: Variable Relevance in Neural Network and Logistic Regression Models. http://dsg.harvard.edu/public/dsg/pubs/ lohnomac98.1.pdf
16. Radetzky A., Nurnberger A., and Pretschner D. (1998). The Simulation of Elastic Tissue in Virtual Medicine Using Neuro -Fuzzy Systems. http://fuzzy.cs.unimagdeburg.de/publications/radet NuernPrets98a.pdf
17. Rodrigues R. and Cabral E. (1999). Human Gait Analysed by an Artificial Neural Network Model. *Proceedings of the IV Brazilian Conference on Neural Networks.* **July 20-22, 1999,** 148-151. www.ele. ita.br/cnrn/artigos-4cbrn/4cbrn_033.pdf
18. Suzuki Y. (1995). Self-Organizing QRS-Wave Recognition in ECG Using Neural Networks. *IEEE Transactions on Neural Networks.* **Vol 6, No 6,** 1469-1477.
19. Theeuwen M, Kappen B. and Neijt J. (1995). Neural Network Analysis to Predict Treatment Out - come in Patients With Ovarian Cancer. http://citeseer.nj.nec.com/83101.html
20. Tsai C.T, Wang J.H., and Sun Y. N. (1998). Liver Stereoscopic Visualis ation by Using Hopfield Neural Nets. *Neural Computing & Applications.* **Vol 7, No 3,** 229-237.
21. Wolff H.S. (1970). *Biomedical Engineering*,. New York, NY: World University Library/McGraw-Hill Book Company.