Diagnosis and Modelling of Alzheimer's Disease through Neural Network Analyses of PET Studies

J.S. Kippenhan and J.H. Nagel

Department of Biomedical Engineering
University of Miami, Coral Gables, FL

ABSTRACT

The back-propagation neural network algorithm was applied to the analysis of PET scans of patients with Alzheimer's Disease (AD). A trained network was able to successfully distinguish PET scans of normal subjects from PET scans of Alzheimer's Disease patients. A new paradigm for back-propagation learning is discussed which emphasizes its similarity to template matching. It is demonstrated that, under certain circumstances, the back-propagation network can be used as an estimation tool, as well as a classification tool, i.e., a trained neural network can indicate the criteria by which its classifications are performed.

INTRODUCTION

The recent wave of interest in neural networks has spread across several disciplines, including the diverse fields of mathematics, psychology, artificial intelligence and signal processing. Neural network algorithms such as the back-propagation network [1] are now being widely applied, even though the means by which they work are often not completely understood.

Back-Propagation Neural Networks: The back-propagation algorithm can be successfully applied with relative ease and generality; these factors have made it a very popular approach to pattern recognition problems. With this algorithm, the user is not required to perform prior statistical analyses or to devise classification rules. The network, in a sense, performs these tasks itself, "learning" to classify by example. During the supervised learning phase, examples of previously-classified patterns are repeatedly presented, and network connection weights are adjusted until an appropriate input-output mapping is achieved.

Functional Imaging and Cerebral Disease: Positron emission tomography (PET) has greatly enhanced studies of the functional effects of various brain disorders. PET images are based on cerebral metabolism, and thus enable regional quantification of brain function. The diagnostic power of PET depends on its ability to indicate deficits or other abnormalities in function.

Recent work [2,3] has been directed toward the discovery of characteristic functional abnormalities in PET scans of patients with Alzheimer's Disease (AD). The abnormalities exhibited in such face of non-gaussian distributions.

analysis [4]. From another perspective, the network learns to synthesize hypervolumes which form regions containing the separate classes [5]. The learning process of networks with back-propagation can be performed by successive transformations of coordinate systems, into a space in which linear discrimination can be performed.

The recent wave of interest in neural networks has spread across several disciplines, including the diverse fields of mathematics, psychology, artificial intelligence and signal processing. Neural network algorithms such as the back-propagation network [1] are now being widely applied, even though the means by which they work are often not completely understood.

Back-Propagation Neural Networks: The back-propagation algorithm can be successfully applied with relative ease and generality; these factors have made it a very popular approach to pattern recognition problems. With this algorithm, the user is not required to perform prior statistical analyses or to devise classification rules. The network, in a sense, performs these tasks itself, "learning" to classify by example. During the supervised learning phase, examples of previously-classified patterns are repeatedly presented, and network connection weights are adjusted until an appropriate input-output mapping is achieved.

Functional Imaging and Cerebral Disease: Positron emission tomography (PET) has greatly enhanced studies of the functional effects of various brain disorders. PET images are based on cerebral metabolism, and thus enable regional quantification of brain function. The diagnostic power of PET depends on its ability to indicate deficits or other abnormalities in function.

Recent work [2,3] has been directed toward the discovery of characteristic functional abnormalities in PET scans of patients with Alzheimer's Disease (AD). The abnormalities exhibited in such face of non-gaussian distributions.

The recent wave of interest in neural networks has spread across several disciplines, including the diverse fields of mathematics, psychology, artificial intelligence and signal processing. Neural network algorithms such as the back-propagation network [1] are now being widely applied, even though the means by which they work are often not completely understood.

Back-Propagation Neural Networks: The back-propagation algorithm can be successfully applied with relative ease and generality; these factors have made it a very popular approach to pattern recognition problems. With this algorithm, the user is not required to perform prior statistical analyses or to devise classification rules. The network, in a sense, performs these tasks itself, "learning" to classify by example. During the supervised learning phase, examples of previously-classified patterns are repeatedly presented, and network connection weights are adjusted until an appropriate input-output mapping is achieved.

Functional Imaging and Cerebral Disease: Positron emission tomography (PET) has greatly enhanced studies of the functional effects of various brain disorders. PET images are based on cerebral metabolism, and thus enable regional quantification of brain function. The diagnostic power of PET depends on its ability to indicate deficits or other abnormalities in function.

Recent work [2,3] has been directed toward the discovery of characteristic functional abnormalities in PET scans of patients with Alzheimer's Disease (AD). The abnormalities exhibited in such face of non-gaussian distributions. 
The above discussion points to the ability of the back-propagation network to perform as an ‘estimation’ tool, in addition to its proven value as a classification tool. In a sense, it can perform ‘unsupervised clustering’. The network algorithm has an advantage over simple, unsupervised clustering in its ability to accommodate cases in which single classes occupy more than one distinct region.

Data was obtained from [F-18] FDG PET scans of normal and AD subjects. Data sets were prepared from studies of fifty-two subjects: twenty-two subjects who had been clinically diagnosed with Alzheimer’s Disease, and thirty age-matched normal subjects. Duara, et al.[2] describe the methods of data preparation. Data for each patient consisted of eight values, representing cerebral glucose metabolism in the eight lobes of the brain: left and right frontal, parietal, temporal and occipital. The mean of each data set was calculated and removed, and the resulting eight-dimensional pattern vectors were used to train a two-layer back-propagation neural network with two hidden units, as shown in Figure 1.

For classification purposes, the network was trained with data from twenty-six subjects (fifteen normal, eleven AD), representing one-half of the above subject group. The trained network was then tested on the remaining half.

RESULTS

The back-propagation neural network classifier proved to be successful in distinguishing normal PET scans from those of patients diagnosed as ‘probable AD’. Within the test group, the trained network’s classification agreed with the clinical diagnosis in 24 of 26 cases. One patient from each class was misclassified, resulting in a sensitivity for AD of 91.5% and a specificity of 93.8%. The accuracy of the network’s classification is compared to that of more traditional methods in Figure 2. As shown in this figure, the neural network is more immune to false positives, as indicated by the higher specificity values, than are the other methods.

To test the network’s usefulness as an estimation tool, the entire group of subjects, with the exception of the two subjects which had been misclassified, was used to train the network. This larger group was used to achieve greater generality. The weight vectors of hidden units were examined after the network had converged to a high degree, i.e. outputs were close to their target values for all subjects.

It should be noted that weight vectors will consistently converge to the same values only under these fairly strict conditions. Results indicate that weight vectors will consistently converge to the same pattern only when (1) all inputs have zero mean, and (2) the network has converged for all input patterns.

For the network trained with the above group of subjects, the weight vectors of the two hidden units consistently converged to the patterns shown in Figure 3. It is interesting to note that each of these patterns contains attributes that had been previously observed clinically, such as asymmetry with left hemiparesis, decrease in parietal function, and sparing of the occipital region[2]. The network can be seen to have “learned” which attributes and combinations of attributes were important for diagnosis.

Figure 4 demonstrates that the mean statistical correlation of both weight vectors with AD patterns are higher than correlations of like weight vectors with normal patterns. Thus, each of these weight vectors can be regarded as ‘features’ likely to be found in AD PET scans. Results such as these may prove to be useful for ‘modelling’ AD and other cerebral diseases, i.e. investigating their physiological nature and origins.

REFERENCES


Jonathan Shane Kippenhan
P.O. Box 248294
Department of Biomedical Engineering
University of Miami
Coral Gables, FL 33124
(305) 284-2442