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Neural Network Models for Biosignal Analysis

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Abstract – Signal analysis provides important clues for diagnosis of disease in many arenas, particularly in cardiology. While each result may give good diagnostic information, a comprehensive decision model requires the combination of results. In the work described here, a neural network model is used to combine various features obtained through signal analysis. The original model is based on electrocardiogram (ECG analysis). This model is extended in two ways: the neural network model is expanded to include other clinical parameters in addition to the ECG and the method is generalized to include other biosignals.

Keywords – Nonlinear analysis, neural network modeling, chaos theory, biosignals, symbolic processing

I. Introduction

Biosignals provide vital information for diagnosis in a number of medical specialties. The most widely used biosignal is the electrocardiogram (ECG) [1]. Traditional use of the ECG focused on the identification of the anomalies in the QRS complex associated with each heartbeat. Each beat is compared to the normal pattern. Variations, denoted arrhythmias, may indicate heart disease, with the specific type indicative of the specific cardiac disorder. Commercial systems for arrhythmia analysis have been used in practice for many years [2]. In addition to arrhythmia analysis, the long-term behavior of the ECG can also yield important diagnostic information. A method in common use, Holter monitoring, records the ECG of an individual for 24-hours or longer by means of a monitoring device that the patient wears while going about normal activities [3]. As well as identifying arrhythmias associated with specific activities, the Holter recordings can yield information of heart rate patterns over a long period. Each of these methods of analysis yields important diagnostic clues. In order to develop a comprehensive decision model, methods are needed to combine the results. Neural networks provide an effective framework not only for combining multiple signal analysis results but also for including other clinical information [4]. In the work described here, basic models are developed for the ECG, followed by methods for extending the approach to other biomedical signals [5].

II. Neural Network Modeling

The neural network model is based on the authors' Hypernet system [6], a non-statistical approach to neural network learning. Hypernet uses an expanded potential function approach in conjunction with the Cohen orthogonal polynomials. The supervised learning algorithm results in a nonlinear network structure with three or more layers. Input parameters can be any type of ordered data. The idea behind potential functions comes from the study of electricity [7]. The basic concept is that each vector $\mathbf{x}_i$, is thought of as a point in space where an electrical charge q_i could be placed. The charge will be positive if $\mathbf{x}_i$ is in class 1 and negative if $\mathbf{x}_i$ is in class 2. The resultant electrostatic potential represents a decision surface. The potential due to n charges is:

$$D(\mathbf{x}) = q_i K(\mathbf{x},\mathbf{x}_i) \quad (1)$$

The potential function $K(\mathbf{x},\mathbf{x}_i)$ of physics varies inversely with $\| \mathbf{x}-\mathbf{x}_i \|$. The corrected decision function is:

$$D'(\mathbf{x}) = \begin{cases} D(\mathbf{x}) + K(\mathbf{x},\mathbf{x}_k) \text{ if } \mathbf{x}_k \text{ is in class 1 and } D(\mathbf{x}_k) < 0 \\ D(\mathbf{x}) - K(\mathbf{x},\mathbf{x}_k) \text{ if } \mathbf{x}_k \text{ is in class 2 and } D(\mathbf{x}_k) > 0 \\ D(\mathbf{x}) \text{ otherwise} \end{cases} \quad (2)$$

$K(\mathbf{x},\mathbf{x}_k)$ can be represented by the expansion

$$K(\mathbf{x},\mathbf{x}_k) = \sum_{i=1}^{n} y_i(\mathbf{x})\, y_i(\mathbf{x}_k) = \mathbf{y}_k^T \mathbf{y} \quad (3)$$

where $\mathbf{y} = \mathbf{y}(\mathbf{x})$ and $\mathbf{y}_k = \mathbf{y}(\mathbf{x}_k)$ and n is the dimension of the vector. Substituting into equation (2)

$$D(\mathbf{x}) = \mathbf{w}^T\mathbf{y}, \quad \text{where} \quad (4)$$

$$\mathbf{w} = \sum_{i=1}^{n} q_i \mathbf{y}_i \quad (5)$$

The weight adjustments to go from $D(\mathbf{x})$ to $D'(\mathbf{x})$ are then

$$\mathbf{w}' = \begin{cases} \mathbf{w} + \mathbf{y}_k & \text{if } \mathbf{y}_k \text{ is in class 1 and } \mathbf{w}^T\mathbf{y}_k < 0 \\ \mathbf{w} - \mathbf{y}_k & \text{if } \mathbf{y}_k \text{ is in class 2 and } \mathbf{w}^T\mathbf{y}_k > 0 \\ \mathbf{w} & \text{otherwise} \end{cases} \quad (6)$$

The most straightforward generalization is from the linear discriminant function to the quadratic:

$$D(\mathbf{x}) = w_0 + \sum w_i x_i + \sum\sum w_{ij} x_i x_j \quad (7)$$

In the more general form:

$$D(\mathbf{x}) = \sum w_i y_i(\mathbf{x}) = \mathbf{w}^T\mathbf{y} \quad (8)$$

where $\mathbf{w}$ is an n-dimensional weight vector and $y_i(\mathbf{x})$ is a set of functions of $\mathbf{x}$.

The method used in Hypernet is a modification of the potential function approach to pattern recognition [8]. Rather than using the Euclidean distance formula, the potential function is used:

$$P(\mathbf{x},\mathbf{x}_k) = \sum_{i=1}^{\infty} \lambda_i \Phi_i(\mathbf{x}) \Phi_i(\mathbf{x}_k) \qquad (9)$$

for k = 1,2,3..., where $\Phi_i(\mathbf{x})$ are orthonormal functions and λ_i are non-zero real numbers. The orthogonal functions of mathematical physics may be used as potential functions [9]. P_1 is computed by substituting the values from the first feature vector for case 1, $\mathbf{x}_1$. Subsequent values for P_k are then computed by

$$P_k = P_{k-1} + r_k P(\mathbf{x},\mathbf{x}_k) \qquad \text{where} \qquad (10)$$

$$r_k = \begin{cases} 1 & \text{If } P_i < 0 \text{ and class 1} \\ -1 & \text{If } P_i > 0 \text{ and class 2} \\ 0 & \text{If } P_i > 0 \text{ and class 1 or } P_i < 0 \text{ and class 2} \end{cases} \qquad (11)$$

The orthonormal functions can in fact be replaced by orthogonal functions, since multiplication by a normalizing factor does not affect the final relative outcome. The functions used in Hypernet are chosen from the set of multidimensional orthogonal functions developed by Cohen, represented by the general class [10]:

$$C_n(x_1,\ldots,x_m) = \frac{m!}{n!(m-n)!} + \sum_{k=1}^{n} \frac{(-1)^k (m-k)!}{(n-k)!(m-n)!} \sum_{i_k=k}^{m} \sum_{i_{k-1}=k-1}^{i_k-1} \cdots \sum_{i_2=2}^{i_3-1} \sum_{i_1=1}^{i_2-1}$$

$$\sum_{p=1}^{k} \frac{x_i^{a(n,i_p)}}{v_{i_p}^{[a(n,i_p)+v_{i_p}]}} \qquad (12)$$

where m is the dimensionality of the data, a_i, i=1,...,k are parameters which may be arbitrarily selected, A is the normalization constant, and v_i, i=1,...,m are assigned values corresponding to the components of the first feature vector.

II. Summary Measures for Biosignals

Summary measures are needed to provide suitable input parameters for the neural network model. Biomedical signals are nonlinear in nature and thus pose additional analytical problems. Chaotic techniques have been shown to be useful in the analysis of these time series, particularly in cardiology [11]. These methods include both graphical representations and numerical summary techniques [12]. The Poincaré differential plot developed by the authors, accompanied by the Central Tendency Measure (CTM) numerical summary have yielded very good results in (ECG) analysis [13], hemodynamic studies [14], and electroencephalogram (EEG) analysis [15]. The Poincaré differential plot is generated by plotting $(T_{i+2}-T_{i+1})$ vs. $(T_{i+1}-T_i)$ where T_n is the n^{th} point in the time series. The central tendency measure is then computed by:

$$CTM = \left[\sum_{i=1}^{t-2} \delta(d_i)\right]/(t-2) \quad \text{where} \qquad (13)$$

where

$$\delta(d_i) = \begin{cases} 1 & \text{if } [(T_{i+2}-T_{i+1})^2+(T_{i+1}-T_i)^2]^{1/2} < r \\ 0 & \text{otherwise} \end{cases} \qquad (14)$$

and r is a specified radius around the origin. A theoretical Poincaré differential plot is shown in Figure 1.

Summary measures provide evidence of the long-term behavior of biosignals. This information alone can yield important diagnostic tools. The diagnostic value can be increased by combining these results with other parameters. Neural networks provide an effective method for development of a multi-parameter model.

III. Applications and Results

A. Cardiac Diagnosis

Diagnosis of cardiac disorders based on ECG analysis consists of two basic types of analyses. The first type focuses anomalies that occur in the QRS complex that occurs in conjunction with each heartbeat. Commercial systems for arrhythmia analysis have been available for many years and are widely used in clinical practice. The second type is based on analysis of the long-term behavior of the biosignal. This long-term behavior is analyzed using nonlinear modeling.

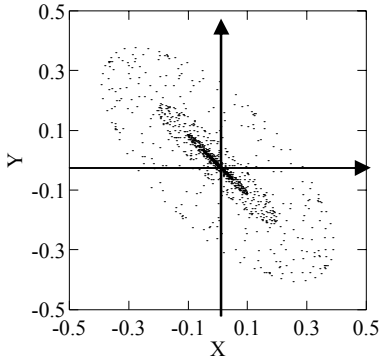

Figure 1: Theoretical Second-Order Difference Plot

As an example, consider evaluation of patients with congestive heart failure. A major component is the Holter recording, which is a twenty-four hour electrocardiogram (ECG) collected by having the patient wear a portable monitor. The patient's ECG is then recorded as he or she goes about normal daily activities. The patient is asked to keep a log so that activities can be correlated with changes in the ECG. Each Holter tape contains in excess of 100,000 points, making it essential to have some method, either graphical or numerical, to summarize the data. The following components give important information.

Event analysis. Holter analysis algorithms that are commercially available check for events such as arrhythmias that may occur during the monitoring. The occurrence of specific arrhythmias are included as input parameters to the neural network.

Summary Analysis. The chaotic analyzer provides the basis for the summary measure for the Holter analysis. A Poincaré differential plot for a congestive heart failure patient is shown in Figure 2. The concentric circles indicate different radii in equation (14). The CTM measure is used as an indicator of the degree of variability in the signal. The results in the form of CTM measures can be used alone or as part of a neural network model that can incorporate multiple CTM measures and also the inclusion of clinical parameters. This model has been successful in both identifying patients with congestive heart failure and also determining predictive factors for survival of these patients [16], shown in Table I.

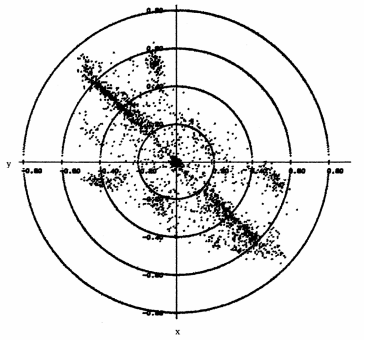

Figure 2: Poincaré Differential Plot of a Patient with CHF

Table I: Neural Network Classification for Congestive Heart Failure

Group 1	Group 2	# g1 g 2	Study	Sen.	Spec.	Accur.
CHF	Other heart disease	32 20	CTM only (r=.01)	69%	91%	74%
CHF	Other heart disease	32 20	CTM+cl*	84%	82%	84%
CHF	Normal	25 27	Combine cl**	80%	89%	85%
CHF	Normal	52 32	Combined cl**	83%	88%	85%
Surviving CHF	Deceased CHF	22 22	CTM+cl***	80*	94%	88%

Parameters
* Edema, rales, HR, BUN
** CTM(r=0.05), CTM(r=0.1), # RR intervals, lowest value CTM > 0.99
*** Symptom status, BUN, orthopnea, dyspnea, HR, edema, functional impairment, PND

B. Relevance of Model to other Biosignals

The CTM measures used in the analysis of Holter tapes is based on the variability of the second-order difference of the R-R intervals. Repeating patterns such as that defined by the QRS complex in the ECG do not exist in many other biosignals. Nonetheless, the Poincaré difference plot and corresponding numerical interpretation using the CTM measure is relevant to other biosignals. Two examples follow: hemodynamic analysis and EEG analysis.

Hemodynamic Studies. As a contrast to the highly structured format of the ECG, we consider a hemodynamic study: the analysis of hemodynamic data collected in an animal model to determine the effect of drugs on the hepatic system. Data were collected to measure the effects of drugs on hepatic flow in a conscious animal model. The apparatus and detailed procedure have been described elsewhere [17]. The data were collected through an implanted, pulsed Doppler ultrasonic flow meter in dogs. A control group was compared with anesthesia (pentobarbital), and two different vasoactive drugs, vasopressin and nicotine, which were injected into the conscious animals. Figure 2 shows a portion of the signal for vasopressin. Note that no discernible pattern is present. Application of the CTM measure was used to determine the degree of variability in the same manner as the Holter tape analysis. Results showed that the variability differed within the four groups in the following manner:

Least Variability ⟶ **Highest Variability**
Nicotine Vasopressin Pentobarbital Control

Electroencephalograms (EEG). As in the hemodynamic studies the EEG has repeating pattern. In addition, EEGs have many channels of input, typically using 22 or more leads that are place symmetrically on the scalp. A recording of ten minutes produces approximately 75,000 points for each lead. The signal consists of spikes that are categorized according to frequency (f) in the following groups that have clinical significance:

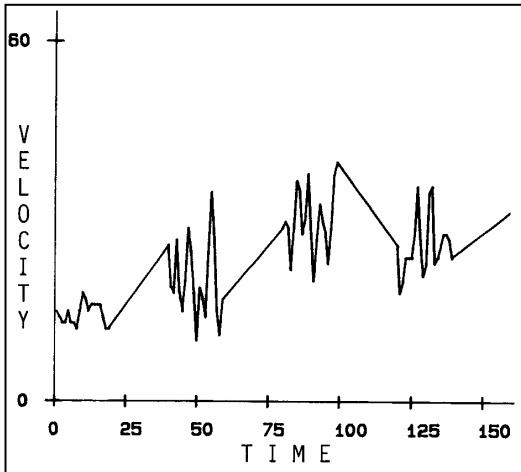

Figure 2: Hemodynamic Study after Injection of Vasopression

Alpha (α): $8 \le f \le 13$ Hz: principle resting rhythm of the brain that is common in awake, resting adults, especially in the occipital lobes. Alpha waves are suppressed when the eyes are open and visual stimulation is present.

Beta (β): $f > 13$ Hz: High frequency beta waves appearing as background activity in anxious subjects.

Delta (δ): $0.5 \le f \le 4$ Hz: Appearing at deep-sleep stages.

Theta (θ): $4 \le f \le 8$ Hz: Appearing at beginning sleep stages.

Depression or absence of expected rhythms in a specific state may indicate abnormality. Focal brain injuries produce abnormal slow waves in the affected regions. Bilateral asynchrony may indicate cortical pathway disturbance. Synchronized spikes and sharp waves are indicative of epileptic seizures. In alert subjects, the frequency of waves increases while the amplitude decreases.

Event Analysis. The definition of isolated events is different from the ECG. An example of an event on an EEG is the occurrence of a wave pattern that does not correspond to the activity level of the patient. These events are identified using coding associated with the EEG recording. Presence or absence of an event is included in the neural network model.

Summary Measures. The CTM measure has been shown to work well on the EEG in defining a level of activity channel by channel. One or more summary measures for each channel are included in the neural network model.

Comparison analysis. Lack of symmetry from corresponding right and left leads can be indicative of disease. Degrees of symmetry are also included in the neural network model [18].

Table II summarizes possible parameters for neural network input nodes for ECG, EEG, and hemodynamic analyses. Although different parameters are used, the neural network architecture does not change, nor does the summary signal analysis methods. For each new application, sufficient training and test sets must be available.

Table II: Neural Network Parameters

Parameter	ECG	EEG	Hemodynamics
CTM*	X	X	X
# RR int.	X		
Min(CTM)	X	X	X
Clinical Info.	X	X	
Symmetry		X	
Events	X	X	

*Multiple CTM measures with differing radii may be included.

IV. Discussion

Diagnostic use of biosignals involves analysis of complex processes. The occurrence of specific events as well as the long-term behavior of the signal offer clues in the diagnostic process. Neural networks form a basis for inclusion of both event occurrence and summary measures in the same model. In addition, neural networks can be used to include clinical parameters in the same model with the biosignal results to form a comprehensive model of disease. This process has been illustrated here for three different types of biosignals, ECGs, EEGs, and hemodynamic studies. Although the input variables change, the same neural network model is applicable, as is the general method of determining signal variability, which is included as one or more input parameters to the neural network. Results in the analysis of congestive heart failure illustrate the clinical utility of this method. Hemodynamic studies provided insight into the behavior of drugs on hepatic blood flow. Early studies on EEGs in dementia patients show promise in the separation of normal controls, mildly impaired patients, and Alzheimer's patients. Additional studies are underway that include models to differentiate among multiple types of dementia, including mixed dementia in which a patient is suffering from more than one type. The neural network model itself has been successfully used in numerous diagnostic areas, including cardiac diagnosis, treatment modalities in lung cancer, and determination of prognostic factors in malignant melanoma.

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