Neuro-Fuzzy Modelling of Heart Rate Signals and Application to Diagnostics

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Abstract: Heart rate variability (HRV) is examined by methods combining neural networks and fuzzy logic. Multiple features are extracted from examples of heart rate data from normal adult subjects, subjects recently suffering from a heart attack, subjects with a history of ischaemic heart disease undergoing a coronary investigation, and subjects in atrial fibrillation. Special attention is given to the analysis of fractal features extracted from heart rate sequences. The methodologies of fuzzy neural networks (FuNN) and evolving fuzzy neural networks (EFuNN) are described and applied to heart rate variability. A description of applications of heart rate variability analysis in medicine is given. The proposed methods can be used for further practical applications in this area.
Key words: heart rate variability, neural networks, fuzzy memberships, evolving networks, fractal measures.

1 Introduction

The analysis of heart rate variability provides important insights into neural control of the heart and has considerable diagnostic utility in assessing patients with autonomic nervous system and cardiovascular disease. In 1973 Sayers [45] and Luczak and Laurig [35] published initial observations which revealed the presence of rhythmic changes within the heart rate signal. Clinical application of the analysis of the heart rate signal in adults was undertaken soon afterwards by Ewing *et al*.

[15] who used RR interval differences to assess autonomic function in subjects with diabetes. In 1978 Wolf *et al.* [51] reported that reduced RR interval variability was associated with a higher heart rate and increased mortality in patients after heart attacks. These findings were confirmed in subsequent studies using statistical [31] and geometric methods [36] of analysis.

Development of frequency domain analysis [1] has emphasized the importance of autonomic control of beat to beat fluctuations and the modulating effect of other neuroendocrine systems such as the renin–angiotensin system. Further studies using power spectrum analysis have revealed the effects of changes in posture and the importance of sympatho–vagal interaction in the autonomic control of heart rate variability [41,43]. These frequency domain measures also proved to be strongly predictive of mortality in patients post heart attack [6].

A collection of sequential heart beat spacings may be viewed as a time series. Several established methods for analyzing time series are available [15,19,48]. We will introduce in detail measures based upon fractal methods. The entire collection of measures will be used as inputs into a fuzzy neural model for classification of subjects with heart disease. Here, we also suggest an adaptive learning methodology utilizing these extended features to enhance heart rate variability data analysis. Knowledge acquisition is developed as a significant part of the modeling which makes the models easy to comprehend.

2
Applications of Heart Rate Variability

In this section, we present some medical diagnostic situations which have been addressed by heart rate variability assessment. Some of these problems are considered in the experimental part of this paper.

2.1
Prognosis After Heart Attack

The measurement of heart rate variability following a heart attack has been shown to be a useful predictor of the future risk of death and life threatening arrhythmias [6,31,39,51]. For all cause mortality heart rate variability has been shown to have similar predictive accuracy to ejection fraction which is an index of overall left ventricular pump function [39]. Both time domain and frequency domain methods of analysis have been used to predict the risk of death after heart attack but analysis of the spectral components has not proved superior to time domain methods. These studies have used specific criteria to separate normal from depressed heart rate variability and have reported positive predictive accuracy of approximately 50% [7].

It remains unknown whether combinations of parameters from the time and frequency domains or non–linear dynamics [20] will improve the predictive accuracy of the assessment of heart rate variability.

2.2
Congestive Heart Failure

Congestive heart failure is a condition characterized by abnormalities of cardiac function and neurohormonal function which is associated with an increased risk of death. Heart rate variability has been reported as impaired in patients with congestive heart failure [9]. Interestingly the decrease in heart rate variability is related to the degree of impairment of left ventricular function which is a predictor of survival [38]. A recent paper has reported that analysis of heart rate variability can also be used to predict survival in patients with congestive heart failure [20].

2.3
Heart transplantation

Patients with a recent cardiac transplantation receive a denervated donor heart and have reduced heart rate variability [2]. Evaluation of heart rate variability in these patients has indicated that at peak exercise an intrinsic mechanism may determine heart rate fluctuations in synchrony with ventilation [5]. More recently non linear methods have been used in patients after heart transplantation with findings of decreased system complexity which most likely relates to the loss of connections between the heart and central nervous system [18]. An initial report has suggested that patients with rejection of the transplanted heart may have increased heart rate variability [44] but this method has not come into general clinical use.

2.4
Cardiac arrest and ventricular arrhythmias

Sudden death may result from a complex interaction between the coronary vasculature, heart muscle injury, and variations in autonomic tone leading to a final common pathway of lethal arrhythmias. Survivors of cardiac arrest have decreased heart rate variability [21] and those with the lowest variability have an increased risk of dying within 1 year [12]. A large prospective study has also shown that decreased short term variability independently increased the risk of cardiac arrest after adjustment for other cardiovascular risk factors [3]. Huikuri *et al*. have reported that spontaneous episodes of ventricular tachycardia, a potentially life threatening arrhythmia, are preceded by lower power in all spectra of the frequency domain [22]. The application of these methods may have potential in directing effective therapy such as implantable cardiac defibrillators in those assessed as being at increased risk although such an approach has yet to be evaluated.

2.5
Atrial Fibrillation

There is limited data regarding heart rate variability in atrial fibrillation as this arrhythmia has previously been regarded as an exclusion criterion for heart rate variability analysis. In patients with atrial fibrillation and valvular heart disease decreased heart rate variability has been associated with an increased risk of mortality or valve replacement surgery [47]. A recent study has reported that heart rate variability in patients with atrial fibrillation is related to vagal tone [49] which suggest analysis of heart rate variability in patients with atrial fibrillation may potentially provide important clinical information of similar value to that of heart variability analysis in patients with sinus rhythm.

2.6
Diabetes

This disease is one of the most common serious metabolic disorders which affects the eyes, kidneys, blood vessels and nerves. Analysis of heart rate variability has been shown useful to detect diabetic autonomic neuropathy and is capable of detecting abnormalities before patients develop symptoms [14]. This is clinically important as the presence of diabetic autonomic neuropathy is a good predictor of increased mortality [13]. The availability of this diagnostic method has proved useful for assessing patients at increased risk from diabetes, making efforts to optimize their management and thereby improving their long term outcome.

2.7
Fetal and Neonatal Assessment

Assessment of the well being of the fetus with the technique of cardiototography is well established in the field of obstetrics. Much of the reported work relates to the early detection of fetal distress with ultrasound methods used to estimate the interbeat interval [11]. More recently nonlinear analytic techniques of phase-space reconstruction and dimensional analysis have been applied to analysis of the normal fetal heart rate with evidence that it may be modeled as a nonlinear or chaotic system [10]. It is possible that application of these more sophisticated techniques may provide earlier identification of fetal distress. A recent study has reported the that prolongation of the QT interval is associated with sudden infant death syndrome [46]. As the autonomic nervous system has important influences on the QT interval it is possible that evaluation of heart rate variability may have a role in this area of investigation.

In section 6, we will present a neuro-fuzzy methodology through comparative analysis of heart rate variability between normal adult subjects and adult subjects

from three heart disease classes: post heart attack, atrial fibrillation, and ischaemic heart disease.

3
HRV Time Series Measures

Time series were constructed from electrocardiograms of subjects by measuring the distance in time between R-R intervals. All subjects were lying supine and quiet during this procedure, but the environment varied among the classes of subjects, as will be discussed in section 6. We say that the resulting series of points is a time series, and we will treat it as such, but this sequence of data points may more adequately be described as an event series. With this connotation, the mechanisms driving the occurrence of each heart beat may be thought of as defining their own time scale. In this way, the measures used to describe each subjects heart beat history, or tachogram, are defined from a particular subject's point of reference, rather than by a fixed arbitrary time scale.

An example of a heart beat series taken from a normal subject is shown in figure 1. The x-axis shows the number of the heart beat event, and the y-axis shows the spacing in milliseconds between heart beats. This view of the heart beat signal yields a different perspective than that obtained by measuring one's pulse. Rather than obtaining only an average value for the event, the rhythms associated with the intrinsic driving forces of the heart beat can be observed and analysed numerically. In our approach, we derive inputs to a neural network model by first calculating traditional inputs from the time and frequency domains, and augment these values by determining parameters taken from fractal analysis.

In our studies, heart beat interval segments of 300 beats were used to calculate all input parameters. Of particular interest, ectopic beats, characterised by a short interval followed by a long interval, were permitted in our analysis. Ectopic beats arise when the initiation of the heart beat occurs from a site other than the sinoatrial node. Rhythms associated with breathing cycles and described by frequency measures are clouded by inclusion of ectopic beats; however, the fractal measures used in this study show no detrimental effect to their inclusion. In addition, the trials described in section 6 include 21 inputs to a fuzzy neural network model that is robust to inaccuracies in the frequency measures.

Our model includes eleven inputs from the time domain, four inputs from the frequency domain, and six inputs from fractal analyis. The inputs are described in table 1 in the numerical order that they are presented in the fuzzy neural model. An intuitive regard for the inputs may be obtained by viewing figure 2. The phase plot shows the evolution of the heart beat intervals over time. The points on this plot are defined by heart beat interval at some time located on the x-axis and the subsequent heart beat interval on the y-axis. This plot represents the trajectory of the heart beat series. If the phase plot is space filling, the heart beat series is more

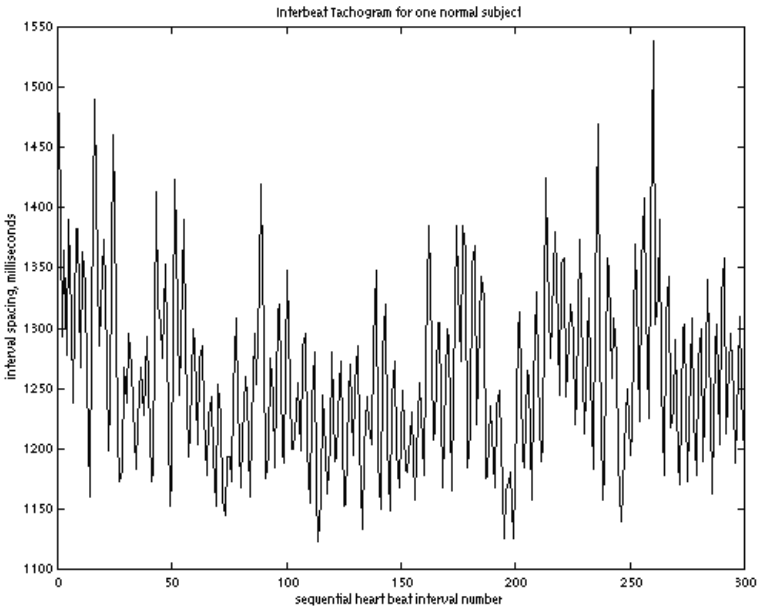

Figure 1 Interbeat Tachogram for a normal subject

chaotic. If the phase plot looks more like a line, the heart beat series is more periodic.

We use fractal measures to capture the information contained in the phase plot. Mandelbrot coined the term fractal and defined it as "a set for which" the fractal dimension "strictly exceeds the topological dimension" [37, page 15]. The fractal dimension is an "index for describing the irregularity of a time series" [19]. The topological dimension of a set is exceeded when the periodicity of the set is interrupted by 'self-similar' or 'self-affine' structures occurring over several measurement scales. Self similar structures are formed by transforming all dimensions of each point of a set by a single real ratio. Self-affine structures are formed by transforming each point of a set by a collection of real ratios of number equal to the Euclidean dimension of the point [37], a mapping of $X \rightarrow R(x)$ where

$$X = (x_1 \ldots . x_\delta \ldots . x_E) \quad \text{and}$$

$$R(x) = R(x_1 \ldots . x_\delta \ldots . x_E) = (x_1 r_1 \ldots . x_\delta r_\delta \ldots . x_E r_E) \quad \text{and}$$

$(r \ldots . r_\delta \ldots . r_E)$ are positive real ratios [37].

Table 1 Features used in the Fuzzy Neural Network Classification Model

1.	Fractal Dimension, D, over low wave numbers, 1 through 11
2.	Fractal Dimension, D, over high wave numbers, 11 through 64
3.	Fractal Dimension, D, over all wave numbers, 1 through 64
4.	Fractal Deviation, sigma, over low wave numbers, 1 through 11
5.	Fractal Deviation, sigma, over high wave numbers, 11 through 64
6.	Fractal Deviation, sigma, over all wave numbers, 1 through 64
7.	Percentage of the absolute magnitude of the second derivative of intervals exceeding 50 milliseconds
8.	Percentage of the absolute magnitude of the first derivative of intervals exceeding 30 milliseconds
9.	Mean of intervals
10.	Standard deviation of intervals
11.	Root mean square of differences between adjacent intervals
12.	Mean difference between adjacent intervals
13.	Standard deviation of differences between adjacent intervals
14.	Ratio of the mean and standard deviation of differences between adjacent intervals
15.	Percentage of adjacent intervals where the first interval is 50 milliseconds longer than the second
16.	Percentage of adjacent intervals where the second interval is 50 milliseconds longer than the first
17.	Percentage of the power spectra in the low frequency range between 0.04 and 0.15 per beat
18.	Percentage of the power spectra in the high frequency range between 0.15 and 0.4 per beat
19.	Ratio of the power spectra in the high frequency range to the low frequency range
20.	Number of times the R-R interval first derivative changes directions
21.	Ratio of the power spectra in the low frequency range to the high frequency range

References for Table 1
Measures 1 through 6 [19]
Measures 7 through 19 and 21 [48]
Measure 20 [35]

Fractal measures have been successfully applied to the classisfication of foetal heart rate measures [16]. In both this reference and this paper, the fractal dimension, D, is obtained following the method defined by Higuchi, 1988 [19]. The variation in the heart beat interval may be viewed at different time scales by creating several series of points at increasing intervals between points. For example, the first series of points is sampled from the original series at every point. Referring to the fractal plot shown in figure 2, the point on this plot located above

wave number 1 represents the sum of the absolute value of the differences between the points from this series. The second series is sampled at every other point.

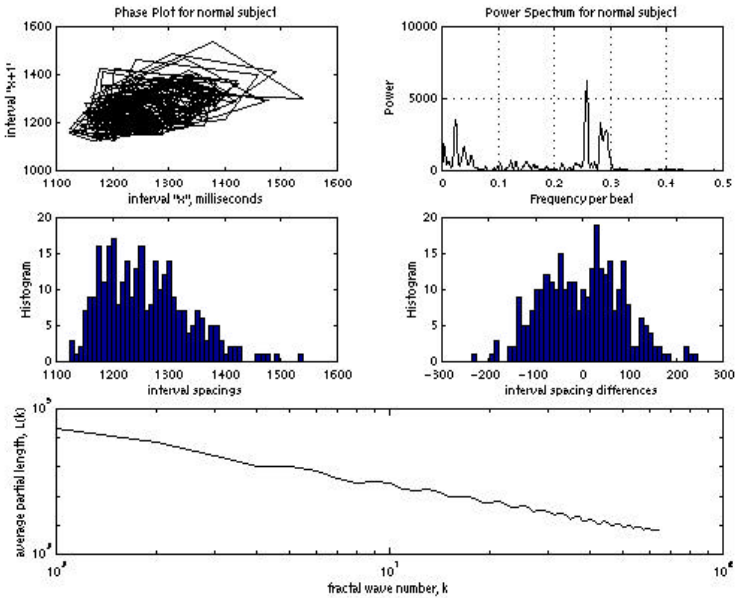

Figure 2 Representations of Measures for HRV analysis for this subject contains sharp frequency spectral features in addition to fractal characteristics [52]. Frequency spectral features are also observed by viewing the power spectra, shown in the second plot of figure 2, which indicates the relative strengths of regularities in the data over a range of sampling frequencies.

Again, the sum of the absolute value of the differences between the points from this series are obtained. Since two series may be defined taking every other point, one starting at the first point and one starting at the second point of the original series, the sum from each of these possibilities is averaged to form the average partial length, L(k). We chose an upper limit of the wave number, k, to be 64, since our data sets were limited to 300 points.

The fractal dimension, D, is obtained by associating an exponential relationship between the wave number and the average partial length. In the method used here to determine the fractal dimension, the calculation of the average partial length includes a division by the wave number, k, yielding a fractal dimension in the range of negative one to negative two. If the time series being analysed is smooth, the fractal dimension will be negative one, corresponding to purely periodic data. If the complexity of the data changes as quickly as the viewing perspective, or the

wave number, then the fractal dimension will be negative two, corresponding to random data. When the fractal dimension is somewhere between these two extremes then the data set ranges from quasi-periodic to chaotic.
In figure 2, the bottom plot shows the fractal wave number plotted versus the average partial length, both on logarithmic scales. If the relationship between these two variables was strictly exponential, the fractal plot shown would be a straight line. Rather, the line is wavy indicating that the heart rate variability data for this subject contains sharp frequency spectral features in addition to fractal characteristics [52]. Frequency spectral features are also observed by viewing the power spectra, shown in the second plot of figure 2, which indicates the relative strengths of regularities in the data over a range of sampling frequencies.

In the fractal analysis, we make use of this information by assessing the goodness of fitting the fractal plot, plotted logarithmically, to a straight line. For the subjects with good parasympathetic, respiratory feedback, spectral resonances are strong at frequencies of 0.25 to 0.33 per heart beat interval. Heart rate data from most normal subjects and some subjects after heart attacks displayed this behavior. For these subjects, we observed the ripples in their fractal plot beginning at wave number 3 or 4. This results in a high value for the fractal deviation at low wave numbers, listed as feature 4 in table 1.

For subjects without good respiratory control, true for most subjects in the chronic ischaemic heart disease class and some of the subjects in the post heart attack class, the high frequency resonance is absent in the power spectra from their heart rate data. Here, we observed the low frequency spectra resonances at about 0.10 to 0.11 per heart beat, perhaps due more to sympathetic feedback from the circulatory system [48], to be manifested in the fractal plot by a break in the straight line at a wave number of 10 or 11. This results in a difference between the measured fractal dimension at low versus high wave numbers, features 1 and 2 in table 1, and a high value for the fractal deviation over all wave numbers, feature 6 in table 1.

In addition to the spectral features just described, the fractal parameters indicate the level of irregularity [37] present in the heart rate data at different scales [17]. We have used these parameters alone [34] to distinguish between three of the classes presented here, normal subjects, chronic ischaemic heart disease subjects, and subjects in atrial fibrillation. With the addition of the class of subjects following a heart attack, we have observed similarities in the fractal parameters between specific subjects from this class and normal subjects. The differences between some of the subjects from these groups were resolved by the addition of features indicative of the range and distribution of heart beat interval differences, features 7, 8, 15 and 16 in table 1, and a feature obtained from the number of local minima and local maximums in the data [35], feature 20 in table 1.

4
Fuzzy Neural Networks (FuNNs)

Fuzzy neural networks are neural networks that realise a set of fuzzy rules and a fuzzy inference machine in a connectionist way [23]. FuNN is a fuzzy neural network introduced in [28] and developed in [30].

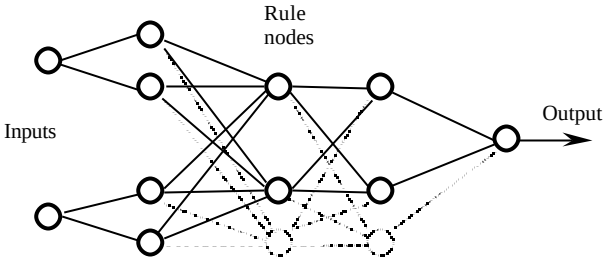

Figure 3 A FuNN structure of 2 inputs (input variables), 2 fuzzy linguistic terms for each variable (2 membership functions). The number of the rule (case) nodes can vary. Two output membership functions are used for the output variable.

It is a connectionist feed-forward architecture with five layers of neurons and four layers of connections. The first layer of neurons receives the input information. The second layer calculates the fuzzy membership degrees to which the input values belong to predefined fuzzy membership functions, e.g. small, medium, large. The third layer of neurons represents associations between the input and the output variables, fuzzy rules. The fourth layer calculates the degrees to which output membership functions are matched by the input data, and the fifth layer does defuzzification and calculates exact values for the output variables. A FuNN has features of both a neural network and a fuzzy inference machine. The number of neurons in each of the layers can potentially change during operation through growing or shrinking. The number of connections is also modifiable through learning with forgetting, zeroing, pruning and other operations.

The membership functions (MF) used in FuNN to represent fuzzy values, are of triangular type, the centres of the triangles being attached as weights to the corresponding connections. The MF can be modified through learning that involves changing the centres and the widths of the triangles.

Several training algorithms have been developed for FuNN [28,30]:

(a) A modified back-propagation (BP) algorithm that does not change the input and the output connections representing membership functions (MF);
(b) A modified BP algorithm that utilises structural learning with forgetting, i.e. a small forgetting ingredient, e.g. 10^{-5}, is used when the connection weights are updated;
(c) A modified BP algorithm that updates both the inner connection layers and the membership layers. This is possible when the derivatives are calculated separately for the two parts of the triangular MF. These are also the non-monotonic activation functions of the neurons in the condition element layer;
(d) A genetic algorithm for training;

(e) A combination of any of the methods above used in a different order.

Several algorithms for rule extraction from FuNNs have been developed and applied [28,29,30]. One of them represents each rule node of a trained FuNN as an IF-THEN fuzzy rule.

FuNNs have several advantages when compared with the traditional connectionist systems, or with the fuzzy systems:

(a) They are both statistical and knowledge engineering tools.
(b) They are robust to catastrophic forgetting, i.e. when they are further trained on new data, they keep a reasonable memory of the old data.
(c) They interpolate and extrapolate well in regions where data is sparse.
(d) They accept both real input data and fuzzy input data represented as singletons (centres of the input membership functions).

The above listed features of FuNNs make them universal statistical and knowledge engineering tools. Many applications of FuNNs have been developed and explored so far: pattern recognition and classification; dynamical systems identification and control; modelling chaotic time series and extracting the underlying chaos rules, prediction and decision making [28]. A FuNN simulator is available as part of a comprehensive soft- computing environment FuzzyCOPE/3 from the WWW: http://kel.otago.ac.nz/software/FuzzyCOPE3/.

5
Evolving Fuzzy Neural Network (EFuNN)

5.1
A general description

EFuNNs are FuNN structures that evolve according to the ECOS principles. EfuNNs adopt some known techniques from [4,8,32] and from other known NN techniques, but here all nodes in an EFuNN are created during (possibly one-pass) learning. The nodes representing MF (fuzzy label neurons) can be modified during learning. As in FuNN, each input variable is represented here by a group of spatially arranged neurons to represent a fuzzy quantisation of this variable. For example, three neurons can be used to represent "small", "medium" and "large" fuzzy values of the variable. Different membership functions (MF) can be attached to these neurons (triangular, Gaussian, etc.). New neurons can evolve in this layer if, for a given input vector, the corresponding variable value does not belong to any of the existing MF to a degree greater than a membership threshold. A new fuzzy input neuron, or an input neuron, can be created during the adaptation phase of an EFuNN.

The EFuNN algorithm, for evolving EFuNNs, has been presented in [24 - 27]. Here a new rule node rn is connected (created) as the EFuNN evolves and its input

and output connection weights are set as follows: W1(rn)=EX; W2(rn) = TE, where TE is the fuzzy output vector for the current fuzzy input vector EX. In case of "one-of-n" EFuNNs, the maximum activation of a rule node is propagated to the next level. Saturated linear functions are used as activation functions of the fuzzy output neurons. In case of "many-of-n" mode, all the activation values of rule (case) nodes, that are above an activation threshold of *Ahtr*, are propagated further in the connectionist structure.

5.2 The EFuNN learning algorithm

Here, the EFuNN evolving algorithm is given as a procedure of consecutive steps:

1. Initialise an EFuNN structure with a maximum number of neurons and zero-value connections. Initial connections may be set through inserting fuzzy rules in a FuNN structure. FuNNs allow for insertion of fuzzy rules as an initialisation procedure thus allowing for prior information to be used prior to the evolving process (the rule insertion procedure for FuNNs can be applied [28,30]). If initially there are no rule (case) nodes connected to the fuzzy input and fuzzy output neurons with non-zero connections, then *connect* the first node rn=1 to represent the first example EX=x_1 and set its input W1(rn) and output W2 (rn) connection weights as follows:

<*Connect a new rule node rn to represent an example EX*>: W1(rn)=EX;W2(rn) = TE, where TE is the fuzzy output vector for the (fuzzy) example EX.

2. WHILE <there are examples> DO

Enter the current, example xi, EX being the fuzzy input vector (the vector of the degrees to which the input values belong to the input membership functions). If there are new variables that appear in this example and have not been used in previous examples, create new input and/or output nodes with their corresponding membership functions.

3. Find the normalised fuzzy similarity between the new example EX (fuzzy input vector) and the already stored patterns in the case nodes j=1,2,…,rn:

Dj= sum (abs (EX - W1(j))/ 2) / sum (W1(j))

4. Find the activation of the rule (case) nodes j, j=1:rn. Here radial basis activation function, or a saturated linear one, can be used on the Dj input values i.e. A1 (j) = radbas (Dj), or A1(j) = satlin (1 – Dj).

5. Update the local parameters defined for the rule nodes, e.g. age, average activation as pre-defined.

6. Find all case nodes j with an activation value A1(j) above a sensitivity threshold *Sthr*.

7. If there is no such case node, then <*Connect a new rule node*> using the procedure from step 1.

ELSE

8. Find the rule node *inda1* that has the maximum activation value (ma*xa1)*.

9. (a) in case of one-of-n EFuNNs, propagate the activation *maxa1* of the rule node *inda1* to the fuzzy output neurons. Saturated linear functions are used as activation functions of the fuzzy output neurons:

A2 = satlin (A1(inda1) * W2)

(b) in case of many-of-n mode, only the activation values of case nodes that are above an activation threshold of *Athr* are propagated to the next neuronal layer.

10. Find the winning fuzzy output neuron *inda2* and its activation *maxa2*.

11. Find the desired winning fuzzy output neuron *indt2* and its value *maxt2*.

12. Calculate the fuzzy output error vector: Err=A2 - TE.

13. IF (*inda2* is different from *indt2)* or (abs(Err (inda2)) > *Errthr*) <*Connect a new rule node*>

ELSE

14. Update: (a) the input, and (b) the output connections of rule node k=inda1 as follows:

(a) Dist=EX-W1(k); W1(k)=W1(k) + lr1. Dist, where *lr1* is the learning rate for the first layer;

(b) W2(k) = W2 (k) + *lr2*. Err. maxa1, where *lr2* is the learning rate for the second layer.

15. Prune rule nodes j and their connections that satisfy the following fuzzy pruning rule to a pre-defined level representing the current need of pruning:

IF *(node (j) is OLD) and (average activation A1av(j) is LOW) and (the density of the neighbouring area of neurons is HIGH or MODERATE) and (the sum of the incoming or outgoing connection weights is LOW) and (the neuron is NOT associated with the corresponding "yes" class output nodes (for classification tasks only))* THEN *the probability of pruning node (j) is HIGH*

The above pruning rule is fuzzy and it requires that the fuzzy concepts as OLD, HIGH, etc. are defined in advance. As a partial case, a fixed value can be used, e.g. a node is old if it has existed during the evolving of a FuNN from more than 60 examples.

16. END of the while loop and the algorithm

17. Repeat steps 2-16 for a second presentation of the same input data or for ECO training if needed.

6
Diagnostic Modelling and Classification using FuNN

Our first approach to modelling the characteristics of heart rate variability within and among the classes of subjects in our study utilises the fuzzy neural network (FuNN) architecture.

6.1

Class Descriptions

We include four classes of subjects in our model. First, normal subjects are defined as those that are not exhibiting any heart disease symptoms. Normal subjects necessarily enjoy the most relaxed situation of all the classes in this study, since they are lying quietly in a private room, and they are volunteering for this study at their convenience. Next, we include a class of subjects who have recently, within one or two days previous, suffered a heart attack. Data for these subjects is drawn from electrocardiogram data while each subject is an in-patient in the hospital. Our next class of subjects is derived from outpatients undergoing a coronary investigation in the catheterisation laboratory to determine the effects of one of two types of drugs, esmolol or nicardipine. These subjects suffer from ischaemic heart disease and are in a highly stressful situation since they are in a brightly lit room, and they have a catheter probe inserted into their leg. Finally, we have a class of subjects who are outpatients receiving treatment for atrial fibrillation. This condition is a result of loss of control of the sinoatrial node in determining the timing for the next heart beat, as described for ectopic beats.

6.2
HRV Model Description

A FuNN model was structured using 21 inputs described in table 1 [3,35,48] from 300 beat sequences of heart beat intervals. The significance of each of the features in ultimately classifying the input data will be assessed by reviewing the strength of weight connections in section 6.3. Multiple data sets were available from each subject by defining overlapping sequences beginning every 100 heart beats. Each input was normalised between zero and one for the data from all classes and for both training and testing data. After normalisation, each input was fuzzified into three overlapping triangular memberships. The absolute value of the fractal dimension was used before normalisation. For instance, a subject in atrial fibrillation has a heart rate signal that looks random, since the control of the heart beat is derived from a multitude of sites within the heart. This results in a fractal dimension for low and high wave numbers of 2. A subject with ischaemic heart disease from the catheterisation laboratory shows little heart rate variability by fractal measures, and may exhibit a fractal dimension for low wave numbers of 1.4 to 1.5. The result of fuzzification of the fractal dimension for low wave numbers for these two extremes will be a high degree of membership in the low triangular membership for the subject with ischaemic heart disease, a high degree of membership in the high triangular membership for the subject in atrial fibrillation, and and a small degree of membership for both subjects in the medium triangular membership.

The outputs of the FuNN model which indicate the inclusion in one of the four classes are fuzzified in a similar manner. For our model, we represent the outputs using three memberships, again representing low, medium and high values. Each

class example is given a high membership value of one in the output corresponding to its class, and a low membership value of one in the outputs corresponding to all other classes. This protocol does not allow for overlap in qualities among the subjects of two or more classes. In particular, we noticed a strong effect of age within our normal subjects. This age dependence made it difficult to discern diagnostic classification between older normal subjects and the class of subjects previously experiencing a heart attack. This problem led us to an unsupervised EFuNN trial, described in section 7, to identify characteristics about the data sets without specifying an output class.

In our FuNN model, we characterised eleven normal subjects, twenty-one subjects following myocardial infarction, fourteen subjects undergoing a coronary catheterisation, and three subjects during atrial fibrillation. The length of data collection varied among subjects from about fifteen minutes to twenty minutes. Since we used 300 heart beat interval data strings overlapping every 100 beats, we were able to generate a total of 696 data sets. The results of both training and testing our FuNN model are shown in figure 4, together with a detailed delineation of the data used for training and testing, and the portions of data derived from each class. Figure 4 shows the high membership value for each class. As the input data is progressive in time for each subject, variations of the FuNN output show a transient behavior that is indicative of the nonstationarity of the heart rate signal. The results for the testing data from each subject's entire data set are shown in the confusion table, table 2. The test results show a good correct classification for the first three classes. The misclassification for the atrial fibrillation class can be attributed to not having enough test data vectors.

We compared our ability to distinguish between normal and post heart attack subjects with a method that uses symbolic dynamics [50]. This method categorises each R-R interval by its value relative to the average value into four fixed interval windows, and then assigns a symbol (0,1,2,3) to that interval. Then, overlapping sequences of three symbols are constructed, and the frequency of each of the possible 64 sequences is determined. If the R-R intervals fall within only two windows, then the number of possible sequences reduces to eight. Using a value of 100 milliseconds above and below the mean value to define these two windows [50], we compared five post heart attack subjects with five age matched normal subjects. Four out of five of the post heart attack subjects , and three out of five of the normal subjects produced symbolic sequences limited to eight types. One out of five of the post heart attack subjects and two out of five of the normal subjects produced sequences of twenty or more types.

6.3
Knowledge Acquisition from FuNN HRV model

One of the important strengths of a FuNN model is the ability to extract rules that are generated as a result of tuning connection weights between the fuzzified inputs and the fuzzified outputs. For the HRV FuNN model we have chosen 12 hidden

nodes to connect the 63 input fuzzy membership functions, 3 for each of 21 discrete inputs, and the 12 output fuzzy membership functions, 3 for each of the four discrete outputs. The knowledge generated by the FuNN model may be interpreted by viewing Hinton diagrams depicting the relative magnitude of the connection weights between each node, as shown in figure 5 for the connections

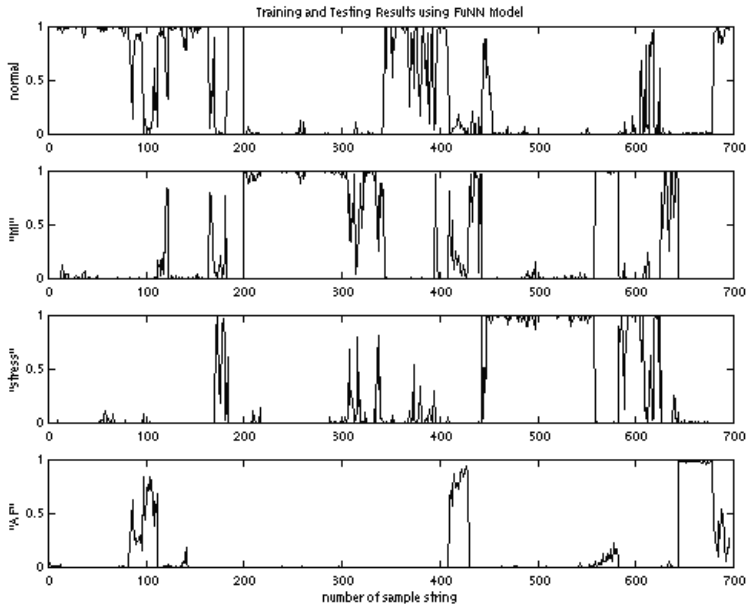

Figure 4 Training and Testing Results using FuNN Model. This figure shows the output associated with a high degree of membership with each of the four classes introduced to the FuNN model in the order, from top to bottom, normal, after heart attack (MI), during a coronary catheterisation (stress), during atrial fibrillation (AF). The records from normal subjects range from 1 through 199, for MI from 200 through 453, for stress from 454 through 643, and from AF from 644 through 696. The records used for training for normal range from 1 through 82 and 143 through 164, for MI from 200 through 305, for stress from 454 through 557, and for AF from 644 through 678. The remaining records were used for testing.

between the fuzzified inputs and the twelve hidden nodes, and in figure 6 for the connections between the hidden nodes and the fuzzified outputs. In these figures, lightly shaded rectangles correspond to positive weight values, and heavier shaded rectangles correspond to negative weight values.

For example, in figure 6, the largest weight activating the high membership for the normal class, row three, is the weight connected to hidden node 12. Following hidden node 12 to figure 5 by looking at row 12, one can view the size and location

of weights for the fuzzified inputs, rendering a degree of importance associated with a particular input feature. Here, a normal output is generated when the fractal dimension for low wave numbers is low, input two, and the fractal dimension over all wave numbers is high, input 9, and the relative number of local minima and maximums is low, input 58.

Table 2 Confusion Table for FuNN model testing outputs. The numbers indicate the ratio of testing subjects from each class yielding on average a high membership in each output class. For example, the number "4/6" in this table means that there were data from a total of six normal subjects for testing the model. Of these, four of the subjects had a majority of their output vectors indicating a high membership in the normal class to a degree greater than 0.5.

	Normal Input	MI Input	Stress Input	AF Input
Normal Output	4/6	4/11	0/5	1/1
MI Output	0/6	5/11	2/5	0/1
Stress Output	0/6	2/11	3/5	0/1
AF Output	0/6	1/11	0/5	0/1

These empirical rules can only be justified when the output of the training data sets appears valid. In this model, the training output for the class of subjects in atrial fibrillation was not valid, as shown in figure 4. This inaccuracy may have occurred because of the low number of examples from this class compared to the other classes. The rules indicating an output of high membership in the class for atrial fibrillation are found by viewing row 12 in figure 6. Hidden nodes 1 and 4 show the largest positive weight values. Turning to figure 5, rows 1 and 4 show that a low membership for the fractal dimension at low wave numbers, and a low membership for the fractal dimension at all wave numbers, and a low membership for the fractal deviation at low wave numbers are important for generating activation of a high membership in the atrial fibrillation class. However, the fractal dimensions for both low and overall wave numbers for subjects in atrial fibrillation have high fuzzified membership values.

7 HRV EFuNN modelling for heart beat interval prediction

Difficulties may arise when attempting to classify data using fuzzy neural networks and other standard neural network and fuzzy logic techniques when the structures of the networks are fixed and do not change with the addition of new data, for

example using a fixed set of input features, using a fixed set of neurons, using a fixed set of membership functions. It is preferable if the HRV model is able to accommodate new data as they become available and adapt its structure in an on line mode. First, if the number of features chosen is too large or redundant, the model may be confused and unable to perform properly [42]. Second, "abrupt non-linear transitions" [17] called bifurcations in the heart rate sequence may render the series non-stationary [19], and features, particularly from the time and frequency domains, may lose their intended significance.

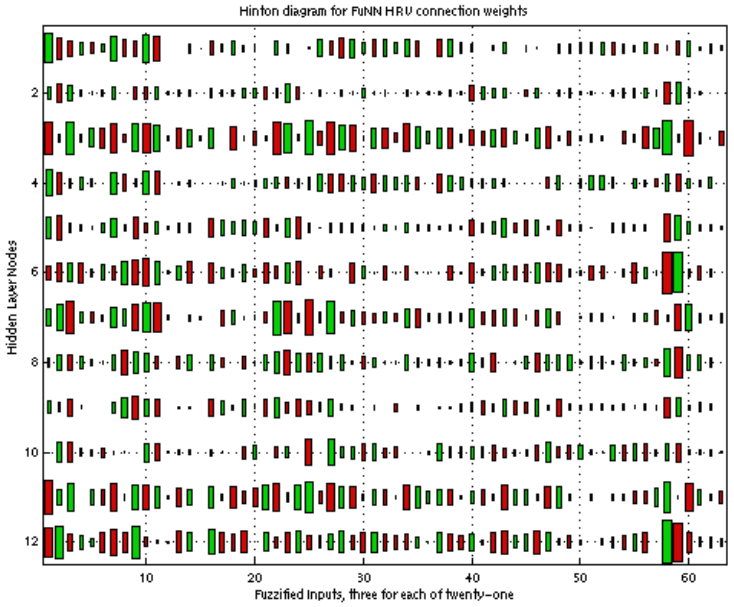

Figure 5 HRV FuNN model Hinton Diagram, fuzzified inputs to hidden nodes. The lightly shaded rectangles represent positive weight values, and the heavier shaded rectangles indicate negative weight values. The relative size of the rectangles indicate the relative magnitude of the weight value. The fuzzified input numbers may be compared to the input features listed in table 1 by associating three memberships, low, medium and high with each input from table 1. For example, input 4 from table 1 is fuzzified and connected to input 10 for membership "low" values, input 11 for membership "medium" values, and input 12 for membership "high" values.

To accommodate the non-stationary nature of heart beat interval data, we are presently formulating an unsupervised learning method, based upon clustering input vectors versus providing output class values. Here, we are using input vectors composed of differences between the current heart beat interval and each of several previous intervals. We have chosen the structure of an EFuNN for this task, as the number of delays defining the size of the input vector may be

dynamically changed to suit the non-stationary characteristics of the data series. Further, the number of clustering nodes for the model may be increased through time to accommodate evolving patterns, or decreased through forgetting to eliminate obsolete patterns.

Eventually, we hope to assess the status of a subject on a beat to beat basis using such an unsupervised learning strategy. This will facilitate a desire assess the condition of patients on an ongoing basis, rather than at a single stationary time [40]. As a first step, we have utilised an eFuNN model to predict the next heart beat interval, given the difference between the preceding interval and each of the previous twenty intervals. By the nature of the eFuNN algorithm, on line training occurred, so that the performance of the system improved as more examples were presented.

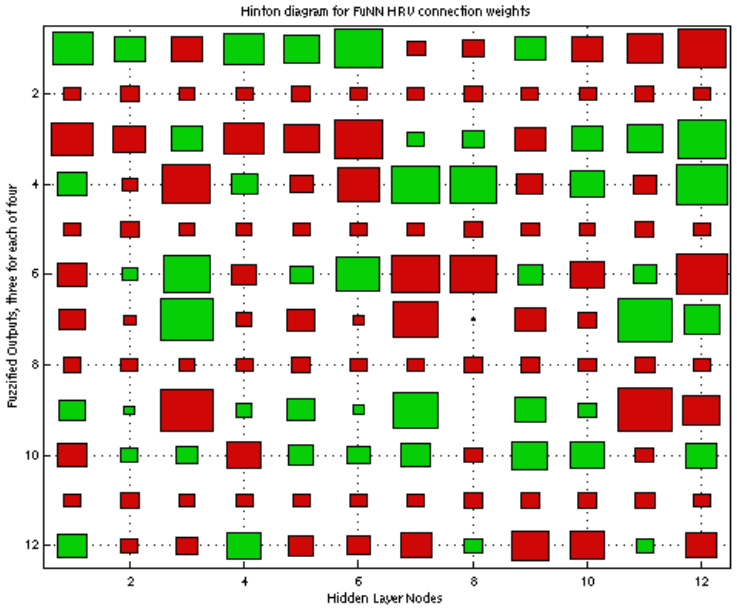

Figure 6 HRV FuNN Model Hinton Diagram, hidden nodes to fuzzified outputs. The lightly shaded rectangles represent positive weight values, and the heavier shaded rectangles indicate negative weight values. The relative size of the rectangles indicate the relative magnitude of the weight value. The fuzzified output numbers for the normal class are 1 for "low" membership, 2 for "medium" membership, and 3 for "high" membership. Likewise, fuzzified output numbers 4, 5, and 6 correspond to "low", "medium", and "high" memberships in the class for recent myocardial infarction; output numbers 7, 8, and 9 correspond to "low", "medium", and "high" memberships in the class for coronary stress test; output numbers 10, 11, and 12 correspond to "low", "medium", and "high" memberships in the class for atrial fibrillation.

The prediction of the heart rate interval using this model is shown in figure 7 for one subject from the chronic ischaemic heart disease class. The first plot shows the prediction of the next heart beat interval as a solid line and the actual next heart beat interval as a dashed line. These curves may be better resolved by viewing the second plot which shows the error defined as the difference between the actual value and the models predicted value. The third plot shows the evolution of nodes in the EFuNN model. In this example, new nodes were generated when the activation of the best match within the rule node layer fell below a sensitivity threshold of 0.6, and also, new nodes were created when the error of the model in predicting the target output exceeded 0.3.

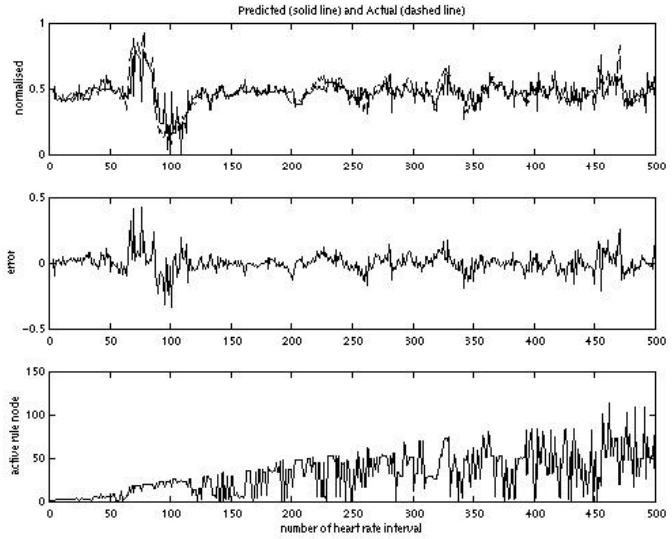

Figure 7 EFuNN Heart Beat Interval Prediction for Coronary Stress Class. The x-axis for all plots shows the sequential heart beat interval number. The first plot depicts the normalised actual heart beat interval as a dashed line and the predicted interval as a solid line. The second plot shows the error in predicting the next interval, thereby testing the model at each step. The third plot shows the rule node that was selected for each input pattern; new nodes were created based upon a sensitivity threshold of 0.6.

The error for this example, as shown in the second plot of figure 7, is greatest between the heart beat intervals 60 through 120. By observation, this location in the heart beat interval sequence represents the most transitory period for this sequence. Improvement to the model in characterising this region may be accomplished by adding additional EFuNN systems in parallel that receive smaller or larger input vectors, and including EFuNN systems in parallel that normalise the input vectors locally, within each vector, as well as globally, across the expected range of the vectors.

8
Conclusion

This paper suggests two neuro-fuzzy models for HRV analysis. The first one is based on a fuzzy neural neural network, FuNN. It produces a good classification rate for the experimental classes of heart disease status if there is sufficient data for training the model. The second model utilises evolving FuNNs, EFuNNs, for dynamically growing models that learn "on-the-fly" the HRV dynamics. Further work is required to determine if these approaches will improve the ability of HRV analysis to predict the future outcome of patients with cardiovascular and nervous system disease.

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