



Original article

Analysis of cardiac health using fractal dimension and wavelet transformation

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Abstract

Analysis of heart rate variation (HRV) has become a popular non-invasive tool for assessing the activities of the autonomic nervous system (ANS). HRV analysis is based on the concept that fast fluctuations may specifically reflect changes of sympathetic and vagal activity. It shows that the structure generating the signal is not simply linear, but also involves nonlinear contributions. These signals are essentially non-stationary; may contain indicators of current disease, or even warnings about impending diseases. The indicators may be present at all times or may occur at random in the time scale. However, to study and pinpoint abnormalities in voluminous data collected over several hours is strenuous and time consuming. This paper presents the continuous time wavelet analysis of heart rate variability signal for disease identification. Fractal dimension (FD) of heart rate signals are calculated and compared with the wavelet analysis patterns. The FD obtained indicates more than 90% confidence interval for all the classes studied.

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1. Introduction

Bio-signals are essentially non-stationary signals; they display a fractal like self-similarity. They may contain indicators of the current disease, or even warnings about impending diseases. The indicators may be present at all times or may occur at random in the time scale. However, to (study and) pinpoint anomalies in voluminous data collected over several hours is strenuous and time consuming. Therefore, computer based analytical tools for in-depth study and classification of data over day long intervals can be very useful in diagnostics.

The ECG belongs to the above category of bio-signals. It displays an apparent periodicity (of about 60–80 bpm in a healthy adult), but is not exactly periodic. The heart rate of a healthy individual is not a constant even under serene condi-

tions; it keeps on changing throughout the day, which can be directly monitored from the ECG. Disease and affliction do influence the heart rate, and therefore, the pattern and the range of heart rate variability would contain important information about the robustness of health, types of diseases etc. Therefore, classification based on the spread and pattern of this parameter can provide useful insight about the type and intensity of the affliction.

Heart rate variation (HRV) is a useful signal for understanding the status of the autonomic nervous system (ANS). HRV refers to the variations in the beat intervals or correspondingly in the instantaneous heart rate (HR). The normal variability in HR is due to autonomic neural regulation of the heart and the circulatory system [28]. The balancing action of the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) branches of the ANS controls the HR. Increased SNS or diminished PNS activity results in cardio-acceleration. Conversely, a low SNS activity or a high PNS activity causes cardio-deceleration. The degree of variability in the HR provides information about the functioning

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of the nervous control on the HR and the heart's ability to respond.

Past 20 years have witnessed the recognition of the significant relationship between ANS and cardiovascular mortality including sudden death due to cardiac arrest [5,13,14,29,30]. Owing of the significant results obtained in this area a task force was set up by the Board of European Society of Cardiology and was co-sponsored by the North American Society of Pacing and Electrophysiology. Numerous numbers of papers appeared in connection with HRV related cardiologic issues [2,9,12,15] reiterates the significance of HRV in assessing the cardiac health. The interest in the analysis of heart rate variability (HRV), (that is, the fluctuations of the heart beating in time,) is not new. Furthermore, much progress was achieved in this field with the advent of low cost computers with massive computational power, which fueled many recent advances.

HRV is a non-invasive measurement of cardiovascular autonomic regulation. Specifically, it is a measurement of the interaction between sympathetic and parasympathetic activity in autonomic functioning. There are two main approaches for analysis: time domain analysis of HRV for standard deviation of normal to normal intervals (SDNN); and frequency domain analysis for power spectrum density (PSD). The latter provides high frequency (parasympathetic activity), low frequency (sympathetic activity) and total power (sympathetic/parasympathetic balance) values. Spectral analysis is the most popular linear technique used in the analysis of HRV signals [1,21,35]. Spectral power in the high frequency band (HF: 0.15–0.5 Hz) reflects respiratory sinus arrhythmia (RSA) and, thus, cardiac vagal activity. Low frequency (LF: 0.04–0.15 Hz) power is related to baroreceptor control and is mediated by both vagal and sympathetic systems. Very low frequency (VLF: 0.0033–0.04 Hz) power appears to be related to thermoregulatory and vascular mechanisms, and renin-angiotensin systems.

The importance of the biological time series analysis, which exhibits typically complex dynamics, has long been recognized in the area of nonlinear analysis. Several features of these approaches have been proposed to detect the hidden important dynamical properties of the physiological phenomenon. As the statistical characteristics of biological signals often change with time and are typically both highly irregular and non-stationary in many cases, such analysis is so complicated. The nonlinear dynamical techniques are based on the concept of chaos and it has been applied to many areas including the areas of medicine and biology [25–27]. The theory of chaos has been used to detect some cardiac arrhythmia such as ventricular fibrillation [10]. Efforts have been made in determining nonlinear parameters like fractal dimension (FD) for pathological signals and it has been shown that they are useful indicators of pathologies. Methods based on chaos theory have been applied in tracking HRV signals and predicting the onset events such as Ventricular Tachycardia detecting congestive heart failure situations [4]. A novel method based on phase space technique to distinguish nor-

mal and abnormal cases has been proposed for cardiovascular signals [18]. The technique has been extended here to identify the abnormalities of different types.

Recent studies have also stressed the importance of nonlinear techniques to study HRV in issues related to both health and disease. The progress made in the field using measures of chaos has attracted the scientific community to apply these tools in studying physiological systems, and HRV is no exception. There have been several methods of estimating invariants from nonlinear dynamical systems being reported in the literature. Recently, Fell et al. [7]; Radhakrishna et al. [23] have tried the nonlinear analysis of ECG and HRV signals respectively. Also, Paul et al. [20] showed that coordinated mechanical activity in the heart during ventricular fibrillation may be made visible in the surface ECG using wavelet transform. Dingfei et al. [6] have classified the arrhythmia using autoregressive modeling. Mohamed et al. [17] have used nonlinear dynamical modeling in ECG arrhythmia detection and classification. This paper uses the heart rate variability as the base signal for continuous time wavelet analysis. The emerging patterns are compared with known types of diseases. FD of the HRV signal compared with the wavelet transform patterns. FD has unique range for each type of disease.

2. Materials and method

ECG data for the analysis was obtained from MIT-BIH arrhythmia database [31]. Prior to recording, the ECG signals were processed to remove noise due to power line interference, respiration, muscle tremors, spikes etc. The R peaks of ECG were detected using Tompkins's algorithm [19]. The number of dataset chosen for each the eight classes is given in 0. Each dataset consists of around 10,000 samples and the sampling frequency of the data is 360 Hz. The details of ECG data in each class is shown in Table 1. The interval between two successive QRS complexes is defined as the RR interval (t_{R-R}) and the heart rate (beats per minute) is given as:

$$HR = 60 / t_{R-R} \quad (1)$$

In this work, an effort is made to characterize and classify eight different classes with one normal class and seven different cardiac diseases. The HRV signal is extracted from the ECG signal for each class.

2.1. Wavelet analysis

Conventional Fourier Transform techniques are not suitable for analysis of non-stationary signals. The chief limita-

Table 1
ECG data for different cardiac health states

Type	NSR	PVC	CHB	SSS	Ischemic/dilated	AF
Number of datasets	60	60	20	20	20	35

tion of Fourier Transform is that it employs complex exponential functions of infinite duration to represent time domain signals of finite interval. Wavelet analysis, on the other hand, provides a better insight into both the timing and intensity of transient events.

A ‘wavelet’ implies a small wave of finite duration and finite energy, which is correlated with the signal to obtain the wavelet coefficients [24,32]. The reference wavelet is known as the *mother wavelet*, and the coefficients are evaluated for the entire range of the signal interval by translating (shifting) the wavelet continually along the time scale. In the next phase, the wavelet is *dilated* (scaled) to a different width, and the process is repeated. Dilatation is accompanied by modification of amplitude to normalize the energy of the wavelet. The wavelet coefficients are real numbers usually shown by the intensity of a chosen color, against a two dimensional plane with y-axis representing the dilation (scaling factor) of the wavelet, and the x-axis, its translation. In the CWT, the wavelet coefficients are evaluated for infinitesimally small shifts of translation as well as scale factors. That is, the intensity of each pixel in the *scalogram* represents a wavelet coefficient, evaluated separately for a specific pair translation and dilation factors. Thus the resulting color pattern provides a visual indicator of both the size and location of the ‘transient event’ occurring along the time scale [3,33] (Grossman et al., 1990).

For a given wavelet $\psi_{a,b}(t)$, the coefficients are evaluated using Eq. (2):

$$W(a, b) \equiv \int_{-\infty}^{\infty} f(t) \frac{1}{\sqrt{|a|}} \psi^* \left(\frac{t-b}{a} \right) dt \quad (2)$$

where $\psi^* \left(\frac{t-b}{a} \right) = \psi_{a,b}^*(t)$; $a \rightarrow$ scale factor; $b \rightarrow$ translation factor.

The *scalogram* patterns thus obtained also depend on the wavelet chosen for analysis. Bio-signals usually exhibit self-similarity patterns in their distribution, and a wavelet which is akin to its fractal shape would yield the best results in terms of clarity and distinction of patterns. In the present work, the analysis is based on the Morlet wavelet shown in Fig. 1. This wavelet gives good result compared to all the other wavelets.

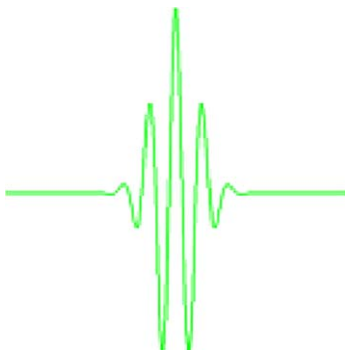


Fig. 1. Morlet wavelet function.

The Morlet wavelet function is given by:

$$h(t) = \exp \left(\frac{-t^2}{2} + jw_0 t \right) \quad (3)$$

where $w_0 = 5.33$.

2.2. Fractal dimension (FD)

The term ‘‘fractal’’ was first introduced by Mandelbrot in 1983 [16]. A fractal is a set of points that when looked at smaller scales, resembles the whole set. The concept of FD that refers to a non-integer or fractional dimension originates from fractal geometry. In traditional geometry, the topological or Euclidean dimension of an object is known as the number of directions each differential of the object occupies in space. This definition of dimension works well for geometrical objects whose level of detail, complexity or ‘‘space-filling’’ is the same. However, when considering two fractals of the same topological dimension, their level of ‘‘space-filling’’ is different, and that information is not given by the topological dimension. The FD emerges to provide a measure of how much space an object occupies between Euclidean dimensions. The FD of a waveform represents a powerful tool for transient detection. This feature has been used in the analysis of ECG and EEG to identify and distinguish specific states of physiologic function [22,34]. Many algorithms are available to determine the FD of the waveform. In this work, algorithms proposed by Higuchi and Katz are implemented for analysis of heart rate signals.

2.2.1. Higuchi’s algorithm

Consider $x(1), x(2), \dots, x(N)$ the time sequence to be analyzed. Construct k new time series x_m^k as :

$$x_m^k = \left\{ x(m), x(m+k), x(m+2k), \dots, x\left(m + \left\lfloor \frac{N-m}{k} \right\rfloor k\right) \right\}$$

for $m = 1, 2, \dots, k$, where m indicates the initial time value, and k indicates the discrete time interval between points, and $\lfloor a \rfloor$ means the integer part of a . For each of the k time series or curves x_m^k , the length $L_m(k)$ is computed by,

$$L_m(k) = \frac{\sum_{i=1}^{\lfloor a \rfloor} |x(m+ik) - x(m+(i-1)k)| (N-1)}{\lfloor a \rfloor k} \quad (4)$$

where N is the total length of the data sequence x , $(N-1) \lfloor a \rfloor k$ is a normalization factor and $a = \frac{N-m}{k}$. An average length is computed as the mean of the k lengths $L_m(k)$ for $m = 1, 2, \dots, k$. This procedure is repeated for each k ranging from 1 to k_{\max} , obtaining an average length for each

k. In the curve of $\ln(L_m(k))$ versus $\ln(1/k)$, the slope of the least-squares linear best fit is the estimate of the FD ($D^{Higuchi}$) [8].

2.2.2. Katz algorithm

Using Katz’s method [11] the FD of a curve can be defined as,

$$D^{Katz} = \frac{\log_{10}(L)}{\log_{10}(d)} \tag{5}$$

where L is the total length of the curve or sum of distances between successive points, and d is the diameter estimated as the distance between the first point of the sequence and the point of the sequence that provides the farthest distance. Mathematically, d can be expressed as $d = \max(\|x(1), x(i)\|)$.

Considering the distance between each point of the sequence and the first, point i is the one that maximizes the distance with respect to the first point. The FD compares the actual number of units that compose a curve with the minimum number of units required to reproduce a pattern of the same spatial extent. FDs computed in this fashion depend upon the measurement units used. If the units are different, then so are the FDs. Katz’s approach solves this problem by creating a general unit or yardstick: the average step or average distance between successive points, a . Normalizing the distances Dis then given by,

$$D^{Katz} = \frac{\log_{10}(L/a)}{\log_{10}(d/a)} \tag{6}$$

3. Surrogate data

The purpose of surrogate data is to test for any nonlinearity in the original data. Nonlinear index FD is computed for several surrogate data series. Their values are compared with that assumed by the nonlinear index computed for the original index [36]. The demonstration of significant difference in nonlinear indices between the original and surrogate data are in keeping with the presence of nonlinear dynamics in the original data.

Surrogate data have Fourier decomposition with the same amplitudes as the empirical data decomposition but with random phase components. This is obtained using the Chaos Data Analyzer. Twenty sets of surrogate data are generated for each of the six classes. FD is obtained for both the original and surrogate data sets. We found that, the surrogate data FD and original data FD, are different from each other by more than 50%. This rejects the null hypothesis and hence the original data contain nonlinear features.

4. Results

The resulting wavelet scalograms, for various types of disease are shown in Fig. 2–7. And the result of the FD for various types of subjects is listed in Table 2.

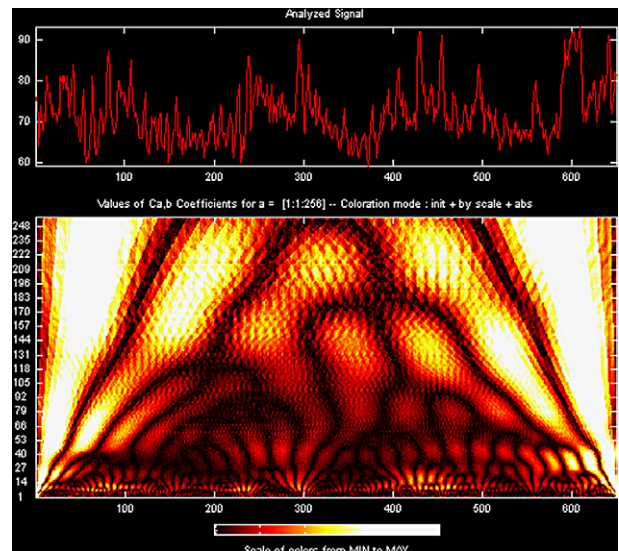


Fig. 2. CWT plot of Normal heart rate.

In the CWT plots shown, white color indicates high value (wavelet) coefficient and black corresponds to low value. As can be seen in the figures, the patterns show continuity in the patterns indicating a continuous variation of heart rate. For Normal cases, the CWT pattern appears to be flowery and regular (Fig. 2). In the *Ectopic beat* abnormality; there would be a sudden impulsive jump in the heart rate. This may be due to a Pre-Ventricular beat in the ECG signal. This is indicated as a sudden surge of radial white lines in the CWT plot, and a spike in the phase space plot (Fig. 3). The black patches indicate the *Bradycardia* and the rest is normal. In the *Atrial Fibrillation* (AF), heart rate signal records highly erratic variability; this is depicted as sudden changes in color (Fig. 4). In *Complete Heart Block* (CHB) cases as the A_V node fails to send electrical signals rhythmically to the ventricles, the heart rate remains low. The pattern is predominantly red (low coefficient value) with very little change in color intensity (Fig. 5). The phase space plot reduces almost

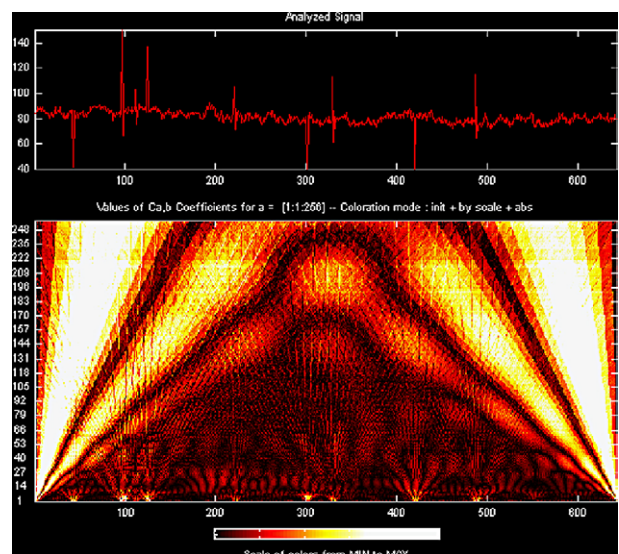


Fig. 3. CWT plot of heart rate with Ectopic beat.

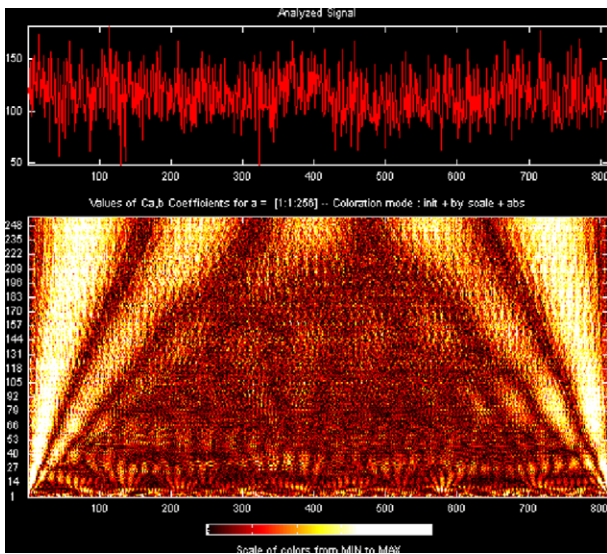


Fig. 4. CWT plot of heart rate with AF.

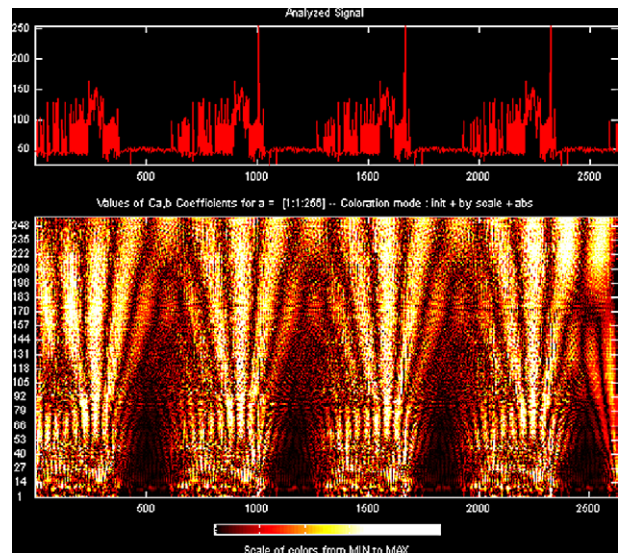


Fig. 6. CWT of heart rate with SSS-III.

to a point, indicating very little change with time. In *Sick Sinus Syndrome-III* (SSS-III, *Bradycardia–Tachycardia*) there is a continuous variation of heart rate between *Bradycardia* and *Tachycardia*, which shows up by way of alternating patches of black (*Brady*) and colored (*Tachy*) patterns (Fig. 6). In the case of *Ischemic/Dilated cardiomyopathy*, the ventricles are unable to pump out blood to the normal degree. Here the HRV is very small. Correspondingly, the color variation too is gradual and periodic (Fig. 7).

In the case of CHB, the fractal dimension $FD1 = 1.24 \pm 0.042$ and $FD2 = 1.41 \pm 0.033$ slightly low value, indicating low variation in the heart rate data. In *Ischemic/Dilated cardiomyopathy*, the variation between the consecutive heart rates is low ($FD1 = 1.32 \pm 0.024$ and $FD2 = 1.52 \pm 0.017$). For SSS-III, the FD is low ($FD1 = 1.21 \pm 0.021$ and $FD2 = 1.36 \pm 0.017$) indicating the inherent periodicity, for AF has too much variation in the heart rate data ($FD1 = 1.21 \pm 0.036$ and $FD2 = 1.39 \pm 0.011$). During *Ec-*

topic beat variation in the heart rate is high ($FD1 = 1.19 \pm 0.043$ and $FD2 = 1.31 \pm 0.019$), finally, for the *Normal* subjects have variation in their heart rates ($FD1 = 1.36 \pm 0.043$ and $FD2 = 1.58 \pm 0.016$). For normal subjects, the FD is high due to the variation being chaotic. And for CHB and *Ischemic/dilated cardiomyopathy*, this FD decreases because the R–R variation is low. And for AF and SSS, this FD value falls further, because the R–R variation becomes erratic or periodic respectively.

5. Conclusion

Heart rate variability (HRV) signal can be used as a reliable indicator of heart diseases. A CWT scalogram of HRV signal can provide a visual pattern, which may provide considerable insight into the nature and pattern of the disease. The scalogram pattern is dependent upon the type of the wavelet used for analysis; which is not examined in this paper.

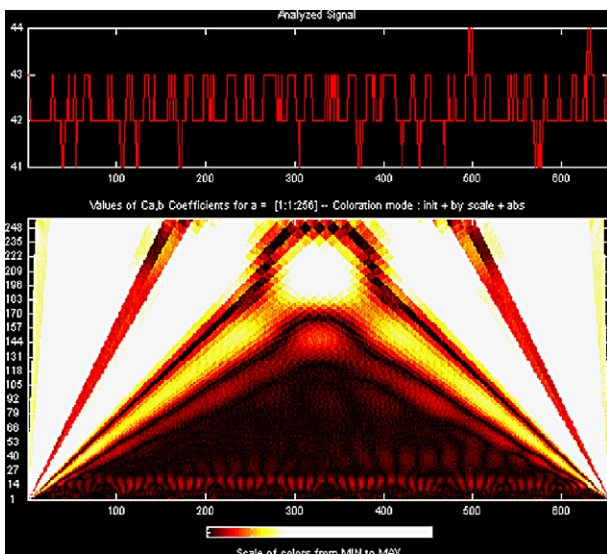


Fig. 5. CWT plot of heart rate with CHB.

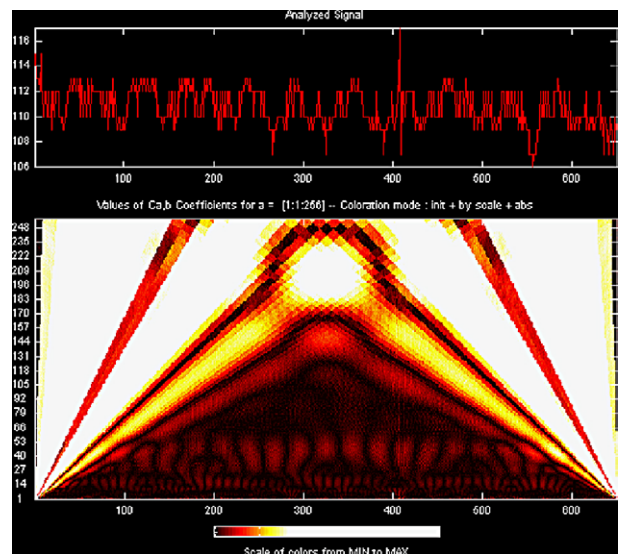


Fig. 7. CWT plot of heart rate with Ischemic/Dilated cardiomyopathy.

Table 2
Results of FD for various types of subjects

Type	NSR	PVC	AF	CHB	SSS	Ischemic	P value
D^{Higuchi} (FD1)	1.36 ± 0.043	1.19 ± 0.043	1.21 ± 0.036	1.24 ± 0.042	1.21 ± 0.021	1.32 ± 0.024	0.072
D^{Katz} (FD2)	1.58 ± 0.016	1.31 ± 0.019	1.39 ± 0.023	1.41 ± 0.033	1.36 ± 0.011	1.52 ± 0.017	0.046

It can be seen that the fractal dimensions D^{Higuchi} and D^{Katz} decreases for the various cardiac abnormalities with respect to the normal subject. This indicates that the irregularity or randomness of the HRV signal is less for cardiac abnormalities. Thus, FDs behave as a reliable indicator of heart diseases with a confidence of more than 90%.

6. Hardware and software specification

To calculate the heart rate and the FD the program is written in MATLAB. The CWT shown in Section 4 are obtained from wavelet toolkit of MATLAB 6.1 version.

7. Mode of availability

The program is freely available (source code, executables for Windows/DOS, documentation, ECG files) on request from the author.

References

- [1] Akselrod S, Gordan D, Ubel FA, Shannon DC, Barger AC, Cohen RJ. Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. *Science* 1981;213:220–2.
- [2] Berger RD, Akselrod S, Gordon D, Cohen RJ. AN efficient algorithm for spectral analysis of heart rate variability. *IEEE Trans Biomed Eng* 1986;33:900–4.
- [3] Chui CK. *Wavelet analysis and its applications*. Boston, MA: Academic Press; 1992.
- [4] Cohen ME, Hudson DL, Deedwania PC. Applying continuous chaotic modeling to cardiac signal analysis. *IEEE Eng Med Biol* 1986;15:97–102.
- [5] Corr PB, Yamada KA, Witkowsky FX. Mechanisms controlling cardiac autonomic function and their relation to arrhythmogenesis. In: Fozzard HA, Haber E, Jennings RB, Katz AN, Morgan HE, editors. *The heart and cardiovascular system*. New York: Raven Press; 1986. p. 1343–403.
- [6] Dingfei G, Srinivasan N, Krishnan SM. Cardiac arrhythmia classification using autoregressive modeling. *Biomed Eng Online* 2002; 1(1):5.
- [7] Fell J, Mann K, Roschke J, Gopinathan MS. Nonlinear analysis of continuous ECG during sleep I. *Reconstr Biol Cybern* 2000;82:477–83.
- [8] Higuchi T. Approach to an irregular time series on the basis of the fractal theory. *Physica D* 1988;31:277–83.
- [9] Kamath MV, Fallen EL. Correction of the heart rate variability signal for ectopics and missing beats. In: Malik M, Camm AJ, editors. *Heart rate variability*. Armonk: Futura; 1985. p. 75–85.
- [10] Kaplan DK, Cohen JR. Searching for Chaos in fibrillation. *Ann New York Acad Sci* 1991;XX:367–74.
- [11] Katz M. Fractals and the analysis of waveforms. *Comput Biol Med* 1988;18(3):145–56.
- [12] Kobayashi M, Musha T. $1/f$ fluctuation of heart beat period. *IEEE Trans Biomed Eng* 1982;29:456–7.
- [13] Levy MN, Schwartz PJ. In: *Vagal control of the heart: experimental basis and clinical implications*. Armonk: Future; 1994.
- [14] Lown B, Verrier RL. Neural activity and ventricular fibrillation. *New Engl J Med* 1976;294:1165–70.
- [15] Malik M, Camm AJ. Components of heart rate variability—what they really mean and what we measure. *Am J Cardiol* 1993;72:821–2.
- [16] Mandelbrot BB. *The fractal geometry of nature*. New York: W.H. Freeman and Co.; 1983.
- [17] Mohamed I Owis, Ahmed H, Abou-Zied, Abou-Bakr M, Youssef, Yasser M. Kadah. Study of features on nonlinear dynamical modeling in ECG arrhythmia detection and classification. *IEEE Trans Biomed Eng* 2002;49(7):733–6.
- [18] Narayana DD, Krishnan SM. Application of Phase space techniques to the analysis of cardiac signals. *Proceedings of IEEE EMBS Conference Atlanta USA*; 1999.
- [19] Pan J, Willis JT. Real time QRS detector algorithm. *IEEE Trans Biomed Eng* 1985;32(3):230–7.
- [20] Paul SA, James NW, Gareth RC, Petter AS, Colin ER. Finding coordinated atrial activity during ventricular fibrillation using wavelet decomposition. *IEEE Eng Med Biol Mag* 2002;21(1):58–61.
- [21] Pomeranz B, Macaulay RJB, Caudill MA, Kutz I, Adam D, Kilborn KM, et al. Assessment of autonomic function in humans by heart rate spectral analysis. *Am J Physiol* 1985;248:H151–H153.
- [22] Pradhan N, Narayana Dutt D. Use of running fractal dimension for the analysis of changing patterns in electroencephalogram. *Comput Biol Med* 1993;23:381–8.
- [23] Radhakrishna Rao KA, Yeragani VK, Narayana Dutt D, Vedavathy TS. Characterizing Chaos in heart rate variability time series of panic disorder patients. In: *Proceedings of ICBME*. India: Biovision 2001; 2001. p. 163–7.
- [24] Rao RM, Bopardikar AS. *Wavelet transforms introduction to theory and applications*. Addison Wesley Longman Inc.; 1998.
- [25] Rajendra AU, Bhat PS, Iyengar SS, Rao A, Dua S. Classification of heart rate data using Artificial Neural Networks and fuzzy equivalence relation. *J Pattern Recognition* 2003;36(1):61–8.
- [26] Rajendra AU, Lim CM, Paul J. HRV analysis using correlation dimension and DFA. *Innovations Technol. Biol. Med. (ITBM-RBM)* 23 (2002) 333–9.
- [27] Rajendra AU, Bhat PS, Iyengar SS, Rao A, Dua S. Classification of heart rate using artificial neural network and fuzzy equivalence relation. *Pattern Recognition* 2003;36:61–8.
- [28] Saul JP. Beat to beat variation of heart rate reflect modulations of cardiac autonomic outflow. *News Physiol Sci* 1990;5:32–7.
- [29] Schwartz PJ, Priori SG. Sympathetic nervous system and cardiac arrhythmias. In: Zipes DP, Jalife J, editors. *Cardiac electrophysiology. from cell to bedside*. Philadelphia: W.B. Saunders; 1990. p. 330–43.
- [30] Task Force of the European Society of Cardiology and North American Society of Pacing and electrophysiology, heart rate variability: standards of measurement, physiological interpretation and clinical use. *Eur Heart J* 1996;17:354–81.
- [31] The MIT-BIH Arrhythmia Database. Available from Beth Israel Hospital, Biomedical Engineering Division Room.
- [32] Vetterli M. Wavelet and filter banks: Theory and design. *IEEE Trans Signal Proc* 1992;40(9):2207–32.

- [33] Vetterli M, Kovacevic J. Wavelets and subband coding. Englewood Cliffs, NJ: Prentice-Hall; 1995.
- [34] Yeragani VK, Sobolewski E, Jampala VC, Kay J. Fractal dimension and approximate entropy of heart period and heart rate: awake versus sleep differences and methodological issues. *Clin Sci* 1998;95:295–301.
- [35] Weissman MW, Markowitz JS, Ouelette R, Greenwald S, Hahn JP. Panic disorder and cardiovascular/cerebrovascular problems. *Am J Psychiatry* 1990;147:1504–7.
- [36] Theiler J, Eubank S, Longtin A, Galdrikian B, Farmer JD. Testing for nonlinearity in time series: the method of surrogate data. *Physica D* 1992;58:77–94.