A DECISION SUPPORT SYSTEM FOR THE DIAGNOSIS OF HEART VALVE DISEASES

İbrahim Türkoğlu, Ahmet Arslan, Erdoğan İlkay

Abstract - **In this paper, a decision support system is presented for interpretation of the Doppler signals of the heart valve diseases based on the pattern recognition. This paper especially deals with the feature extraction from measured Doppler signal waveforms at the heart valve using the Doppler Ultrasound. Wavelet transforms and power spectrum estimate by Yule-Walker AR method are used to feature extract from the Doppler signals on the time-frequency domain. Wavelet entropy method is applied to these features. The back-propagation neural network is used to classify the extracted features. The performance of the developed system has been evaluated in 215 samples. The test results showed that this system was effective to detect Doppler heart sounds. The correct classification rate was about 84% for normal subjects and 95.9% for abnormal subjects.**

Keywords: **Pattern recognition, Doppler heart sounds, feature extraction, wavelet decomposition, Yule-Walker AR, neural networks.**

Özet - **Bu çalışmada, kalp kapak Doppler sinyallerinin değerlendirilmesi için örüntü tanıma esaslı bir karar destek sistemi sunulur. Çalışmada özellikle Doppler Ultrason kullanılarak kalp kapaklarından alınan Doppler sinyallerinin dalga şekillerinden özellik çıkarma ele alınmıştır. Zaman – frekans bölgesinde Doppler sinyallerinden özellik çıkarmak için Dalgacık dönüşümü ve Yule-Walker AR metoduyla güç spektrum yoğunluğu kestirimi kullanıldı. Elde edilen bu özelliklere Dalgacık Entropy metodu uygulandı. Çıkarılan özellikleri sınıflamak için geri yayınım yapay sinir ağı kullanıldı. Geliştirilen sistemin başarımı 215 denek üzerinde denendi. Elde edilen test sonuçlarına göre, geliştirilen sistem Doppler kalp seslerini ayırmak için oldukça etkilidir. Sistemin doğru sınıflama yüzdesi normal olmayan deneklerde %95.9 iken normal deneklerde %84 dür.**

Anahtar Kelimeler - **Örüntü tanıma, Doppler kalp sesleri, dalgacık ayrışımı, Yule-Walker AR, sinir ağları.**

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I. INTRODUCTION

Researches showed that the most of human deaths in the world are due to heart diseases. The heart valve disorders are of importance among the heart diseases. Among them, mitral and aortic valve disorders are the most common ones. For this reason, early detection of heart valve disorders is one of the most important medical research areas [1]. In the today, the used methods for diagnosis of heart valve disorders are non-invasive techniques (electrocardiograms, chest x-rays, heart sounds and murmur from stethoscope, ultrasound imaging and Doppler techniques) and invasive techniques (angiography, transozefagial echocardiograph [2]. However, each method is limited in its ability to offer efficient and thorough detection and characterization [3]. All of these methods are based on experience and information of physician. The researches in this area are focused on improving human-machine interfaces in existing methods. In this way, the cardiologist can understand the output of the examination systems more easily and diagnose the problem more accurately [4].

Doppler techniques are the most preferred because they are completely non-invasive and without risk in the serial studies. The technique has improved much since Satomura first demonstrated the application of the Doppler effect to the measurement of blood velocity in 1959 [5]. In recent years, Doppler technique has found increasing use in the assessment of heart disease [6]. Doppler heart sounds (DHS) are one of the most important sounds produced by blood flow, valves motion and vibration of the other cardiovascular components [7]. However, the factors such as calcified disease or obesity often result in a diagnostically unsatisfactory Doppler techniques assessment and, therefore, it is sometimes necessary to assess the spectrogram of the Doppler shift signals to elucidate the degree of the disease [6]. A major motivation in our work is to aid the diagnosis in such cases. Among Doppler techniques, the most ubiquitous and straightforward are waveform profile indices such as the pulsatility index (PI), Pourcelot or resistance index (RI) and A/B Systolic Diastolic ratio, which are highly correlated and led to highly erroneous diagnostic results [8]. These indices rely on the peak systolic and end-diastolic velocities, with only the PI making use of the mean velocity over the cardiac cycle. More sophisticated methods have also been developed such as the Laplace transform and principal components analysis. However, none of the simple or more complex analytical techniques has yielded an acceptable diagnostic accuracy so as to be commonplace in the vascular clinic [6]. In this study, the developed method is a decision support system and will cause more effective usage of the Doppler technique. Up to now, many attempts have been undertaken to automatically classify Doppler signals using pattern recognition [9,10]. Nevertheless, the studies on the Doppler heart sounds are fairly limited.

This study will introduce the technique that will aid clinical diagnosis, enable further research of heart valve disorders, and provide a decision support system for recognition of heart valve disorders. This study uses the powerful mathematics of wavelet signal processing and entropy, PSD to efficiently extract the features from pre-processed Doppler signals for the purpose of recognizing between abnormal and normal of the heart valve. An algorithm called the decision support system was developed using advanced pattern recognition approximate.

The Doppler heart sounds can be obtained simply by placing the Doppler ultrasonic flow transducer over the chest of the patient. A disadvantage of the Doppler method is that it requires the constant attention of the doctor to detect subtle changes in the DHS [10]. The presented method prevents subtle changes in the DHS from escaping physician's eye by perceiving them, even if the physician does not pay a continuous attention.

The realized study has the stages of decision and evaluation on the contrary the existing diagnosis methods. Thus, the doctor can make a comparison between the diagnoses by the developed method and the diagnoses by the existing methods. If the results are different, the examinations can be repeated or performed more carefully. In this way, the physician can decide more realistically.

The paper is organized as follows. In section II, we review some basic properties of the pattern recognition, the Doppler heart signals, wavelet decomposition, autoregressive methods for the power spectral density, wavelet entropy and neural networks. A decision support system is described in Section III. This new method enables a large reduction of the Doppler signal data while retaining problem specific information which facilitates an efficient pattern recognition process. The effectiveness of the proposed method for classification of Doppler signals in the diagnosis of heart valve diseases is demonstrated in Section IV. Finally Section V presents discussion and conclusion.

II. PRELIMINARIES

In this section, the theoretical foundations for the decision support system used in the presented study are given in the following subsections.

II.1. Pattern recognition

Pattern recognition can be divided into a sequence of stages, starting with feature extraction from the occurring patterns, which is the conversion of patterns to features that are regarded as a condensed representation, ideally containing all-important information. In the next stage, the feature selection step, a smaller number of meaningful features that best represents the given pattern without redundancy is identified. Finally, the classification is carried out, i.e., a specific pattern is assigned to a specific class according to the characteristic features selected for it. This general abstract model, which is demonstrated in Fig.1, allows a broad variety of different realizations and implementations. Applying this terminology to the medical diagnostic process, the patterns can be identified, for example, as particular, formalized symptoms, recorded signals, or a set of images of a patient. The classes obtained represent the variety of different possible diagnoses or diagnostic statements [11]. The techniques applied to pattern recognition use artificial intelligence approaches [12].

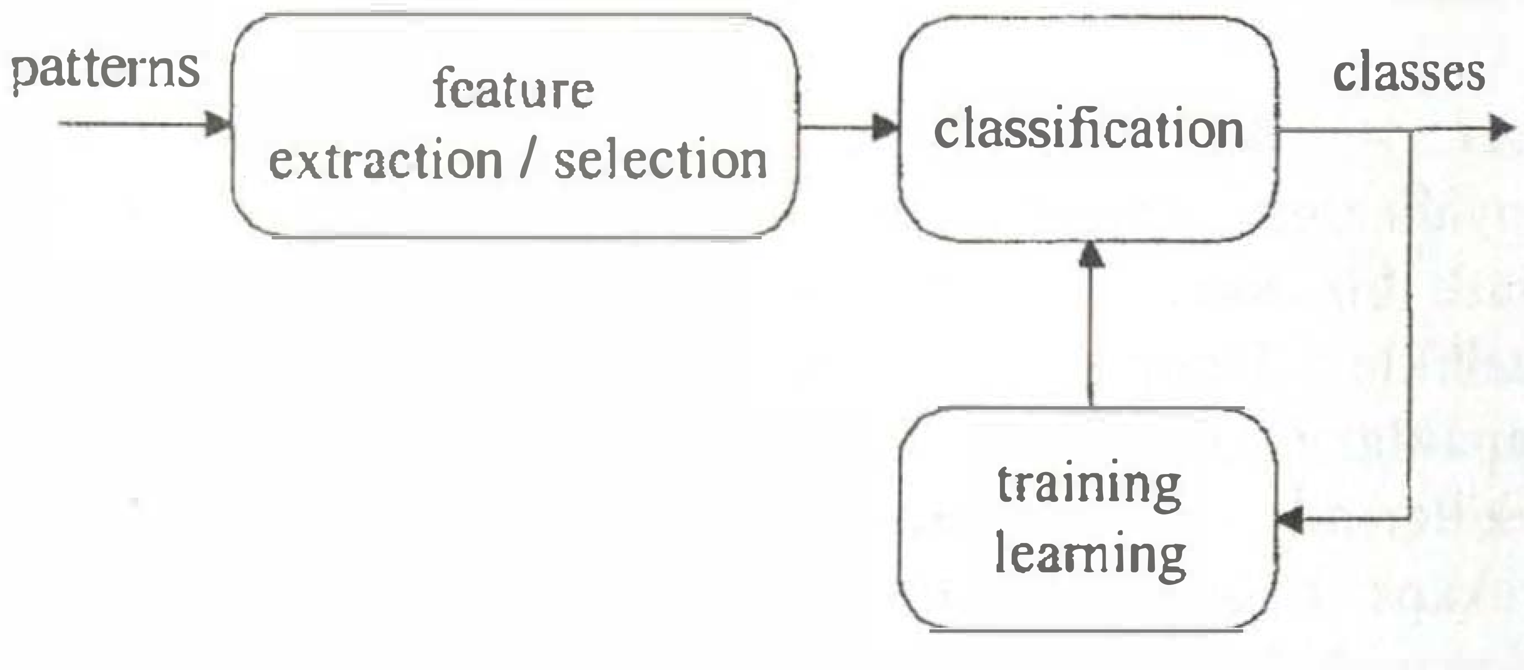

Fig.1. The pattern recognition approach.

II.2. DHS Signals

The audio DHS is obtained simply placing the Doppler ultrasonic flow transducer over the chest of the patient [10]. Figure 2 shows a DHS signal from heart mitral valve. The DHS produced from echoes backscattered by moving blood cells is generally in the range of 0.5 to 10 kHz [13]. DHS signal spectral estimation is now commonly used to evaluate blood flow parameters in order to diagnose cardiovascular diseases. Spectral estimation methods are particularly used in Doppler ultrasound cardiovascular disease detection. Clinical diagnosis procedures generally include analysis of a graphical display and parameter measurements, produced by blood flow spectral evaluation. Ultrasonic instrumentation typically employ Fourier based methods to obtain the blood flow spectra, and blood flow measurements [14].

A Doppler signal is not a simple signal. It includes random characteristics due to the random phases of scattering particles present in the sample volume. Other effects such as geometric broadening and spatially varying velocity also affect the signal [15]. The following is Doppler equation:

$$\Delta f = \frac{2 v f \cos\theta}{c} \qquad (1)$$

Where v equals the velocity of the blood flow, f equals the frequency of the emitted ultrasonic signal, c equals the velocity of sound in tissue (approximately 1540 meter/sec), Δf equals the measured Doppler frequency shift, and θ equals the angle of incidence between the direction of blood flow and the direction of the emitted ultrasonic beam [13].

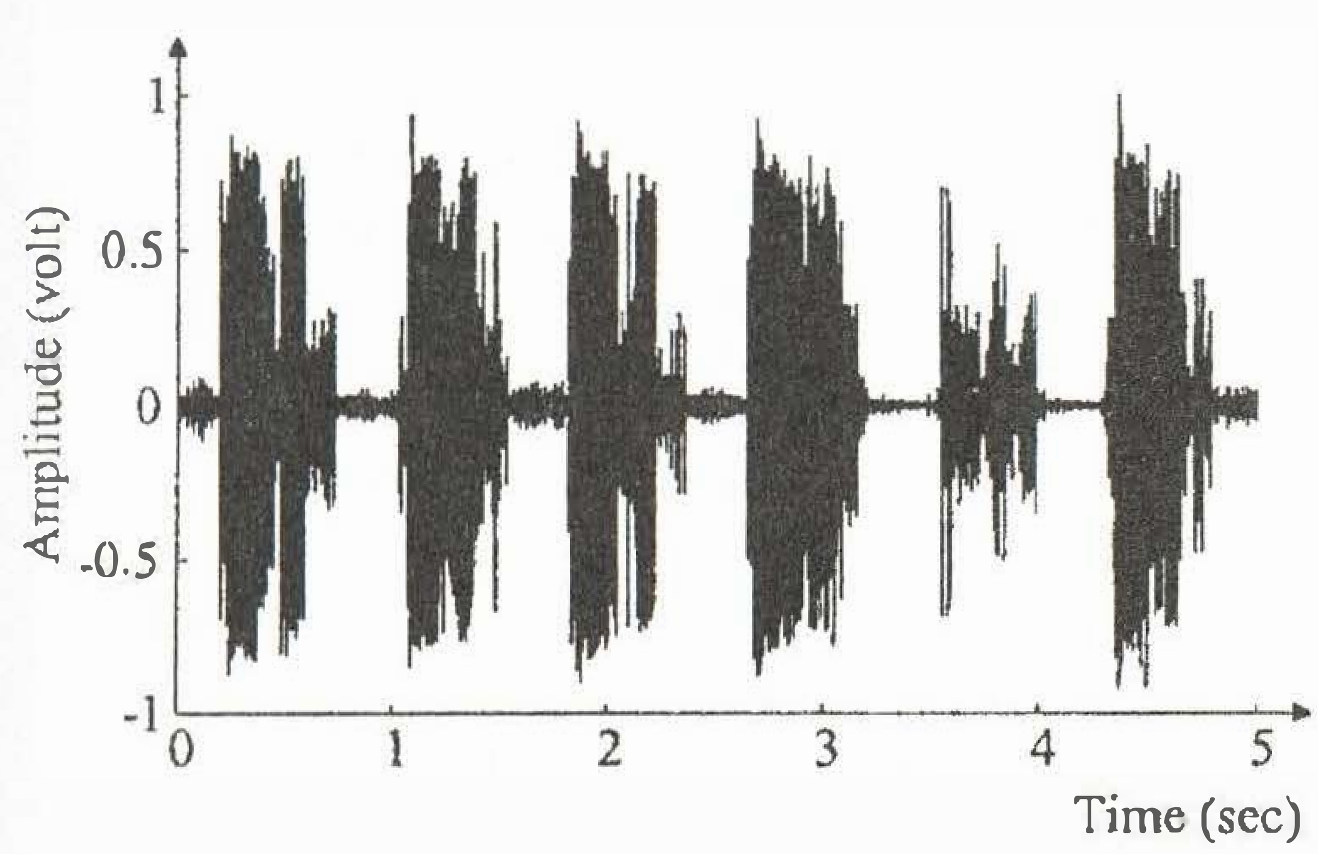

Fig.2. The waveform pattern of the Doppler heart sound.

II.3. Wavelet Decomposition

Wavelet transforms are rapidly surfacing in fields as diverse as telecommunications and biology. Because of tbeir suitability for analysing non-stationary signals, they have become a powerful alternative to Fourier methods in many medical applications, where such signals abound [5,16,17].

The main advantage of wavelets is that they have a varying window size, being wide for slow frequencies and narrow for the fast ones, thus leading to an optimal time-frequency resolution in all the frequency ranges. Furthermore, owing to the fact that windows are adapted to the transients of each scale, wavelets lack of the requirement of stationarity [18].

Wavelet decomposition uses the fact that it is possible to resolve high frequency components within a small time window, and only low frequencies components need large time windows. This is because a low frequency component completes a cycle in a large time interval whereas a high frequency component completes a cycle in a much shorter interval. Therefore, slow varying components can only be identified over long time intervals but fast varying components can be identified over short time intervals. Wavelet decomposition can be regarded as a continuous time wavelet decomposition sampled at different frequencies at every level or stage. The wavelet decomposition function at level m and time location t_m can be expressed as Equation (2):

$$d_m(t_m) = x(t) * \Psi_m\left(\frac{t - t_m}{2^m}\right) \qquad (2)$$

Where Ψ_m is the decomposition filter at frequency level m. The effect of the decomposition filter is scaled by the factor 2^m at stage m, but otherwise the shape is the same at all stages. The synthesis of the signal from its time-frequency coefficients given in Equation (3) can be rewritten to express the composition of the signal x[n] from its wavelet coefficients.

$$\begin{aligned} d[n] &= x[n] * h[n] \\ c[n] &= x[n] * g[n] \end{aligned} \qquad (3)$$

where h[n] is the impulse response of the high pass filter and g[n] is the impulse response of the low pass filter [19].

Wavelet packet analysis is an extension of the discrete wavelet transform (DWT) [20] and it turns out that the DWT is only one of the many possible decompositions that could be performed on the signal. It is therefore possible to subdivide the whole time-frequency plane into different time-frequency pieces. The advantage of wavelet packet analysis is that it is possible to combine the different levels of decomposition in order to achieve the optimum time-frequency representation of the original [5].

II.4. Autoregressive Methods (AR)

The most common parametric method employs autoregressive models (AR) in which it is assumed that a data value at a given time can be predicted from the preceding p data values and a noise term. An advantage of this method is that any power spectrum can be modelled by an AR process of some order p; however, the value of p may exceed the length of the time series. The AR model is written as:

$$x_t = \sum_{k=1}^{p} a_k . x_{t-1} + n_t ; \quad t \geq 1 \tag{4}$$

where x_t represents time samples, a_k are the coefficients of the AR process, p is the model order, and n_t are samples of a stationary white noise process. AR systems can also be described by the power spectrum:

$$\frac{\sigma_p^2 \Delta t}{\left| 1 - \sum_{k=1}^{p} a_k . e^{-j2\pi 2\pi fk} \right|^2} \tag{5}$$

where σ_p^2 is the variance of the noise term, n; f is frequency; Δt is the time between samples [3,19].

II.5. Wavelet Entropy

Entropy-based criteria describe information-related properties for an accurate representation of a given signal. Entropy is a common concept in many fields, mainly in signal processing [21]. A method for measuring the entropy appears as an ideal tool for quantifying the ordering of non-stationary signals. An ordered activity (i.e. a sinusoidal signal) is manifested as a narrow peak in the frequency domain, thus having low entropy. On the other hand, random activity has a wide band response in the frequency domain, reflected in a high entropy value [22]. The types of entropy computing are shannon, threshold, norm, log energy and sure [21].

II.6. Neural Networks

An artificial neural network (ANN) is a mathematical model consisting of a number of highly interconnected processing elements organized into layers, the geometry and functionality of which have been likened to that of the human brain. The ANN may be regarded as the process of learning capabilities inasmuch as it has a natural propensity to store experimental knowledge and to make it available for later use. By virtue of its parallel distribution, an ANN is generally robust, tolerant of faults and noise, able to be generalized well and capable of solving non-linear problems [23]. The Doppler heart sounds, diseased or healthy, may be regarded as an inherently non-linear system due to the absence of the property of frequency preservation as required by the definition of a linear system [24]. Applications of ANNs in the medical field include EMG pattern identification [25], images of human breast disease [26], medical data mining [27], Brachytherapy cancer treatment optimisation [28], interpretation of heart sounds [29], EEG pattern identification [30]; however, to date neural network analysis of Doppler heart sounds is a relatively new approach.

III. METHODOLOGY

Figure 3 shows the decision support system we developed. It consists of three parts: a) Data Acquisition and Pre-processing, b) Feature Extraction, c) Classification Using Neural Network.

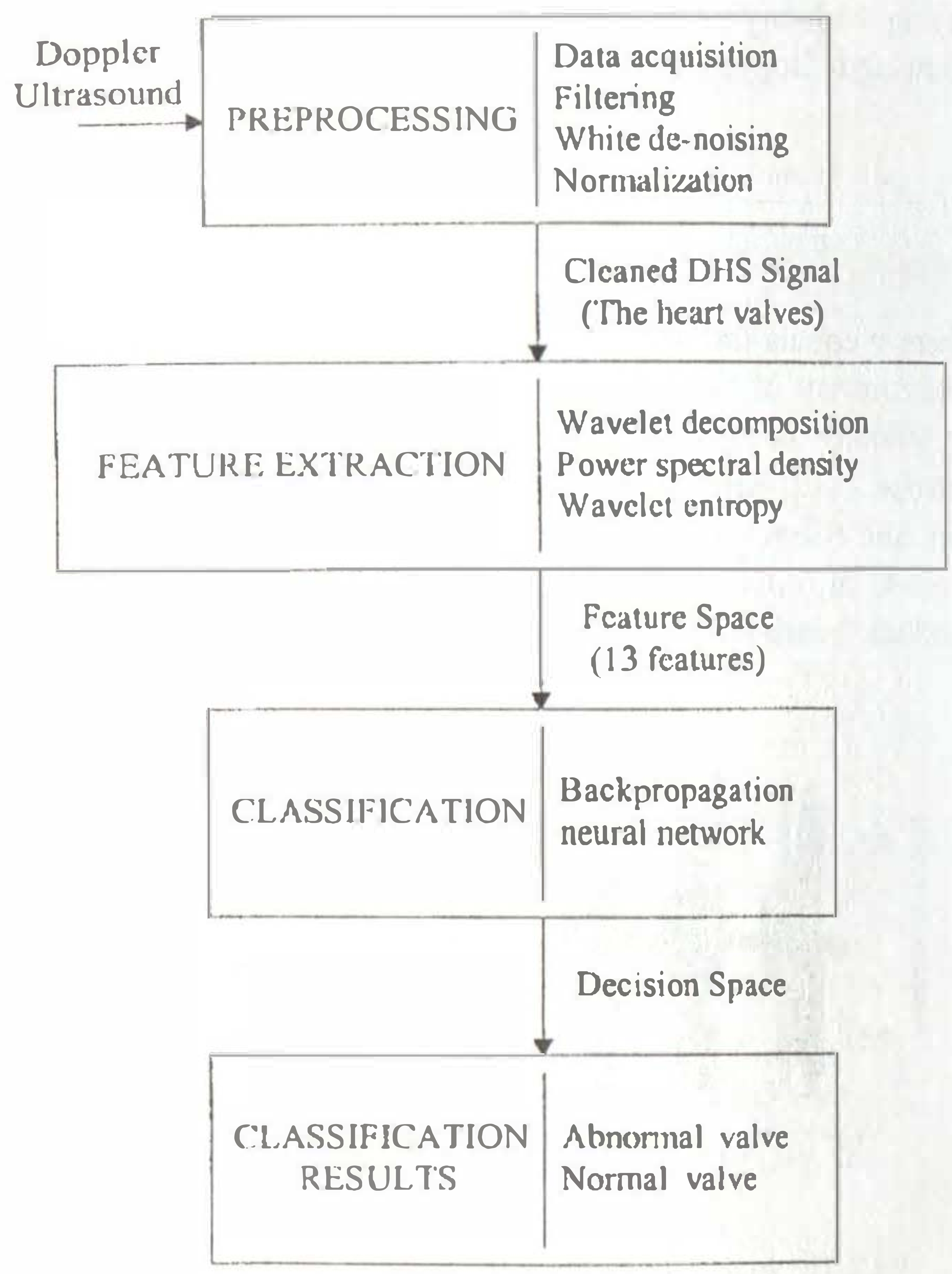

Fig. 3. The algorithm of the decision support system.

III.1. Data Acquisition and Pre-processing

All the original audio DHS signals were acquired from the Acuson Sequoia 512 Model Doppler Ultrasound system in the Cardiology Department of the Firat Medical Center. DHS signals were sampled at 20 kHz for 5 seconds and signal to noise ratio of 0 dB by using a sound card which has 16-bit A/D conversion resolution and computer software prepared by us in the MATLAB (version 5.3) (The MathWorks Inc. Natick, MA, USA). The Doppler ultrasonic flow transducer used (Model 3V2c) was run an operating mode of 2 MHz continuous wave. The Doppler signals of the heart valves were obtained by placing the transducer over the chest of the patient with the aid of ultrasonic image. The digitised data, which has 95 normal and 120 abnormal subjects, were stored on hard disk of the PC. The subject group consisted of 132 males and 83 females with the ages ranging from 15 to 80 years. The average age of the subjects was 48.77 years. Pre-processing to obtain the feature vector was performed on the digitized signal in the following order:

i. Filtering: The reserved DHS signals were high-pass filtered to remove unwanted low-frequency components, because the DHS signals are generally in the range of 0.5 to 10 kHz. The filter is a digital FIR, which is a fiftieth-order filter with a cut-off frequency equal to 500 Hz and window type is the 51-point symmetric Hamming window.

ii. White de-noising: White noise is a random signal that contains equal amounts of every possible frequency, i.e., its FFT has a flat spectrum [19]. The DHS signals were filtered removing the white noise by using wavelet packet. The white de-noising procedure contains three steps [31]:
   1. Decomposition: Computing the wavelet packet decomposition of the DHS signal at level 4 and using the Daubechies wavelet of order 4.
   2. Detail coefficient thresholding: For each level from 1 to 4, soft thresholding is applied to the detail coefficients.
   3. Reconstruction: Computing wavelet packet reconstruction based on the original approximation coefficients of level 4 and the modified detail coefficients of levels from 1 to 4.

iii. Normalization: The DHS signals in this study were normalized using Equation (6) so that the expected amplitude of the signal is no affected from the rib cage structure of the patient.

$$DHS_{signal} = \frac{DHS_{signal}}{\left|\left(DHS_{signal}\right)_{max}\right|} \qquad (6)$$

III.2. Feature Extraction

Feature extraction is the key to pattern recognition so that it is arguably the most important component of designing the decision support system based on pattern recognition since even the best classifier will perform poorly if the features are not chosen well. A feature extractor should reduce the pattern vector (i.e., the original waveform) to a lower dimension, which contains most of the useful information from the original vector. The DHS waveform patterns from heart valves are rich in detail and highly non-stationary. The goal of the feature extraction is to extract features from these patterns for reliable intelligent classification. After the data pre-processing has been realised, three steps are proposed in this paper to extract the characteristics of these waveforms using MATLAB with the Wavelet Toolbox and the Signal Processing Toolbox:

i. Wavelet decomposition: For wavelet decomposition of the DHS waveforms, the decomposition structure, reconstruction tree at level 12 as illustrated in Figure 4 was used. Wavelet decomposition was applied to the DHS signal using the Daubechies-10 wavelet decomposition filters. Thus obtaining two types of coefficients: one-approximation coefficients cA and twelve-detail coefficients cD. A representative example of the wavelet decomposition of the Doppler sound signal of the heart mitral valve was shown in Figure 5.

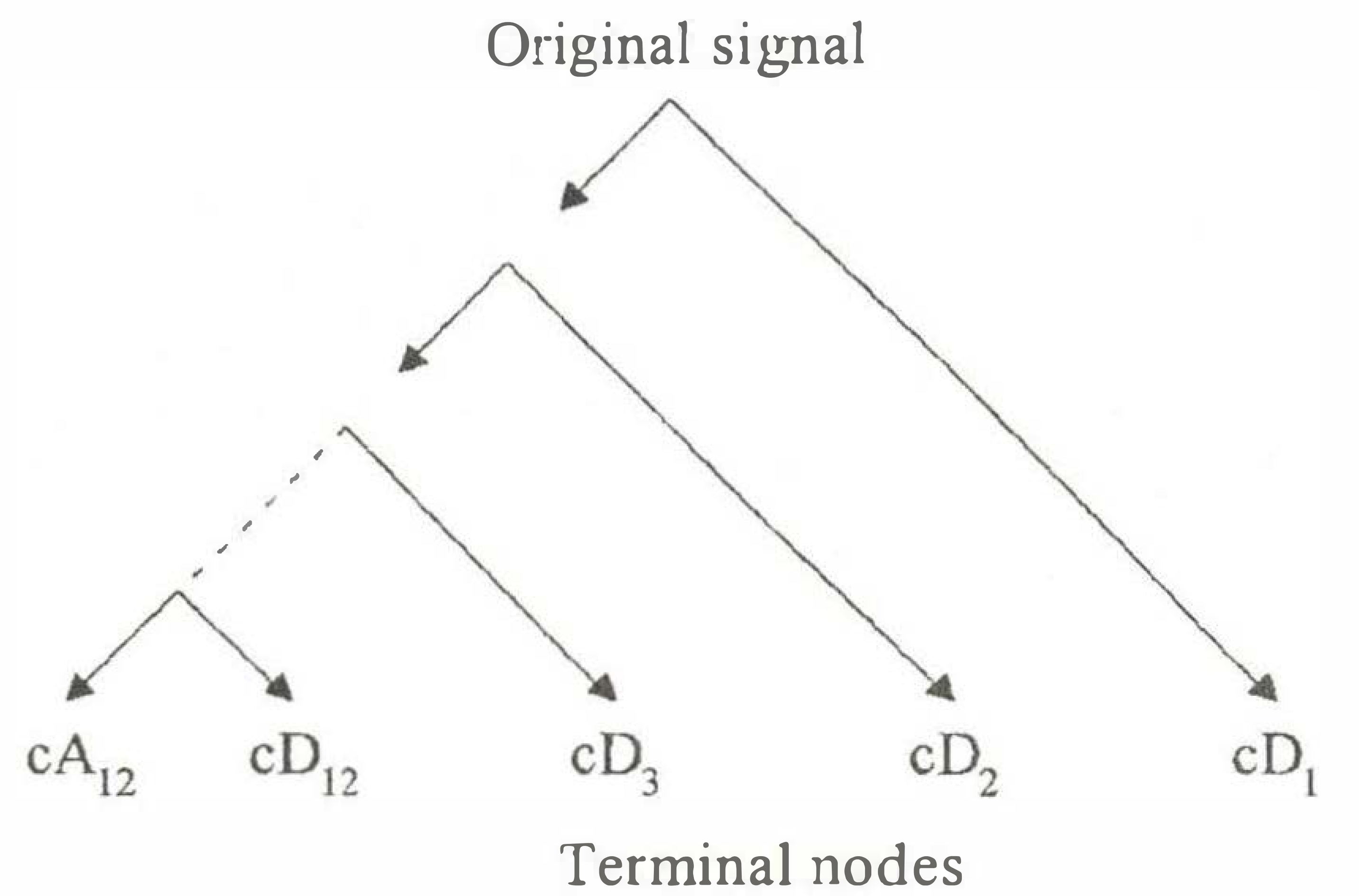

Fig. 4. The decomposition structure in level-12.

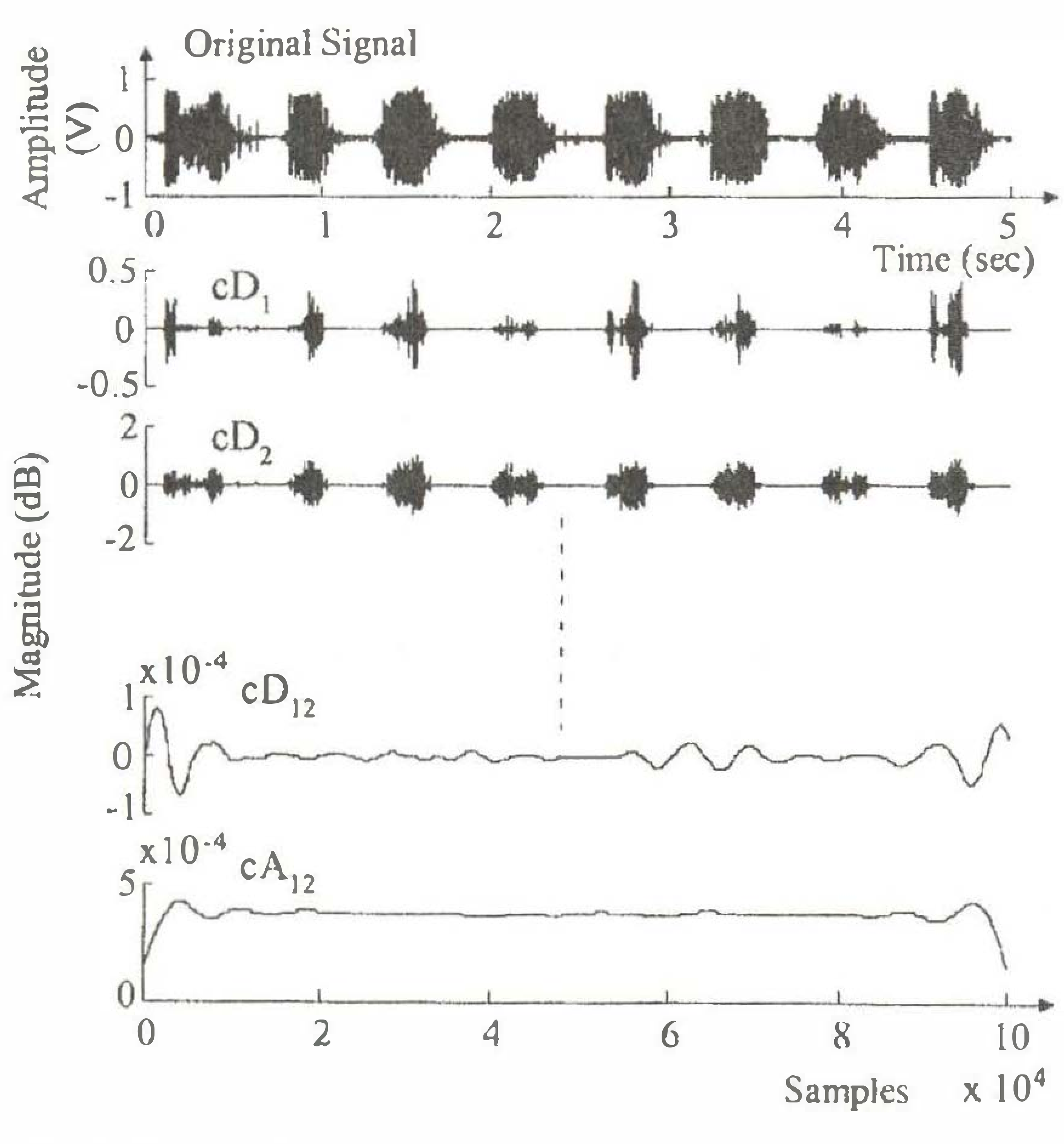

Fig. 5. The terminal node waveforms of wavelet decomposition at twelve levels of the DHS signal.

ii. Power spectral density: The PSD spectrums of terminal nodes were computed using the Yule-Walker AR method. In the AR model, the model order was chosen as p=5 for the all-pole filter and the FFT length was selected as quarter the amount of length of the terminal node signals. A representative example of the PSD spectrum waveform of a terminal node is indicated in Figure 6.

iii. Wavelet entropy: We next calculated the norm entropy as defined in Equation (7) of PSD waveforms.

$$E(s) = \sum_i |s_i|^{3/2} \tag{7}$$

where, s is the PSD spectrum and (s_i) i^{th} coefficients of s. The resultant entropy data, which were normalized with 1/5, were plotted in Fig. 7. The plot of the entropy data includes 13 features obtained from PSD spectrums of 13 terminal nodes. Thus, the feature vector was extracted by computing the wavelet entropy values for each DHS signal.

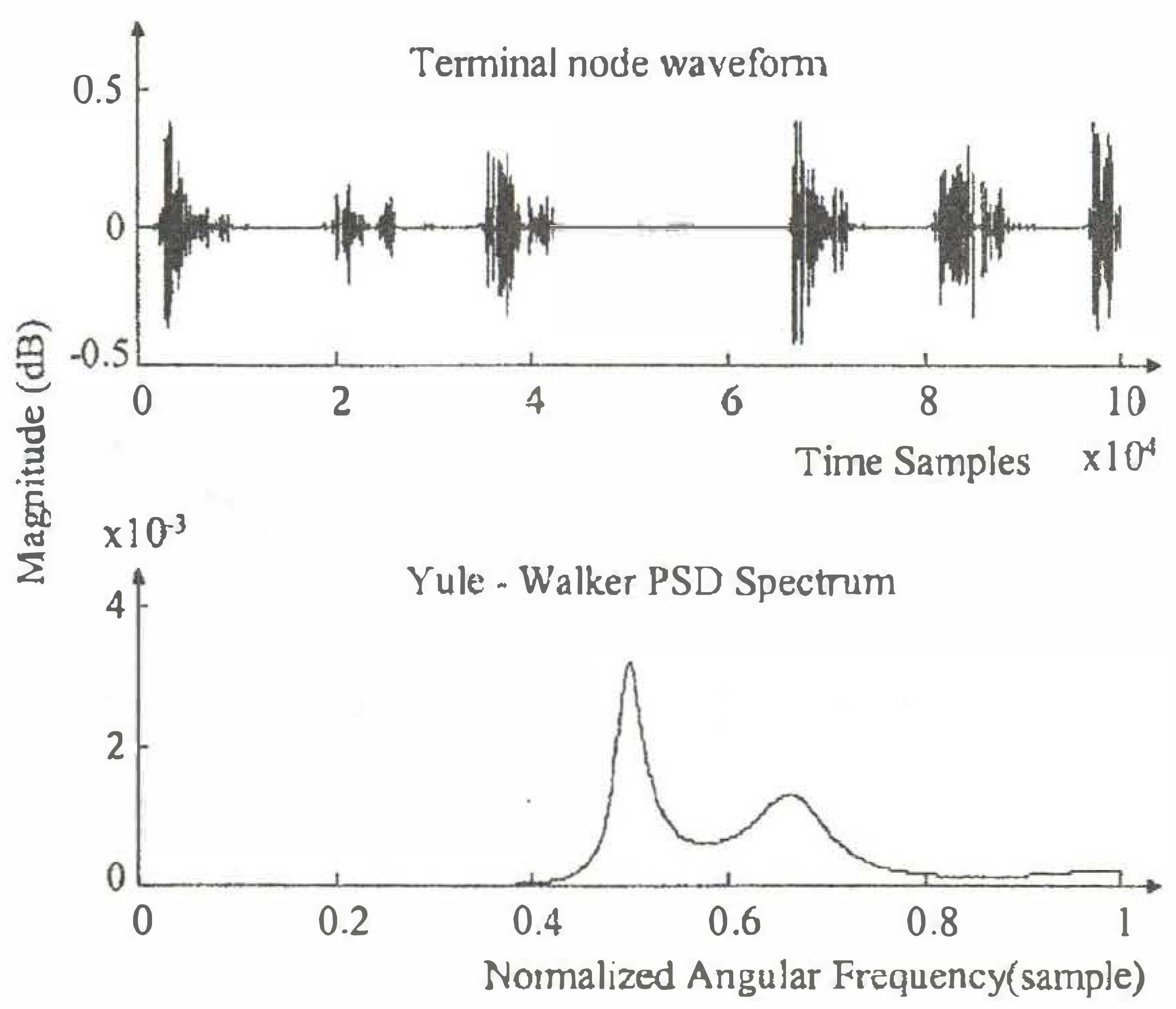

Fig. 6. The PSD spectrum of a terminal node waveform.

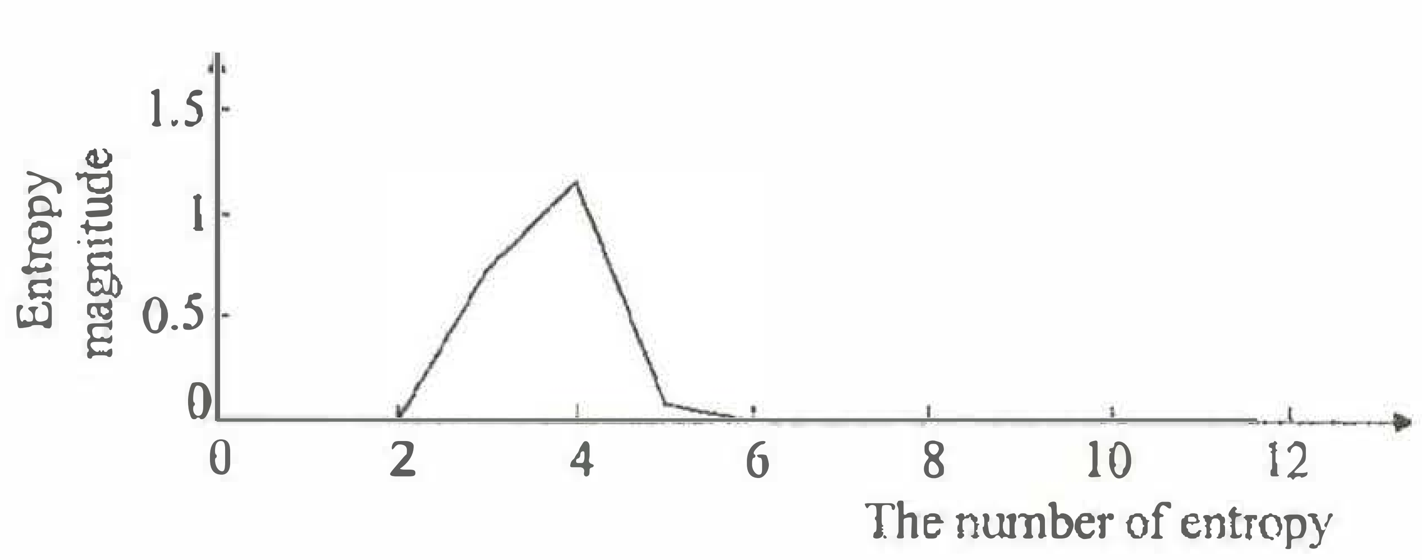

Fig. 7. The wavelet entropy of the DHS signal.

III.3. Classification Using Neural Network

The objective of classification is to demonstrate the effectiveness of the proposed feature extraction method from the DHS signals. For this purpose, the feature vectors were applied as the input to an ANN classifier. The classification by neural network was performed using MATLAB with the Neural Network Toolbox. The training parameters and the structure of the neural network used in this study are as shown in Table 1. These were selected for the best performance, after several different experiments, such as the number of hidden layers, the size of the hidden layers, value of the moment constant and learning rate, and type of the activation functions. Figure 8 shows the ANN training performance.

Table 1. ANN architecture and training parameters

ANN architecture	
The number of layers :	3
The number of neuron on the layers:	Input : 50 Hidden : 5 Output : 2
The initial weights and biases:	The Nguyen-Widrow method
Activation Functions :	Log-sigmoid
ANN training parameters	
Learning rule :	Back-propagation
Adaptive learning rate :	Initial : 0.001 Increase : 1.05 Decrease: 0.7
Momentum constant :	0.95
Sum-squared error :	0.0001

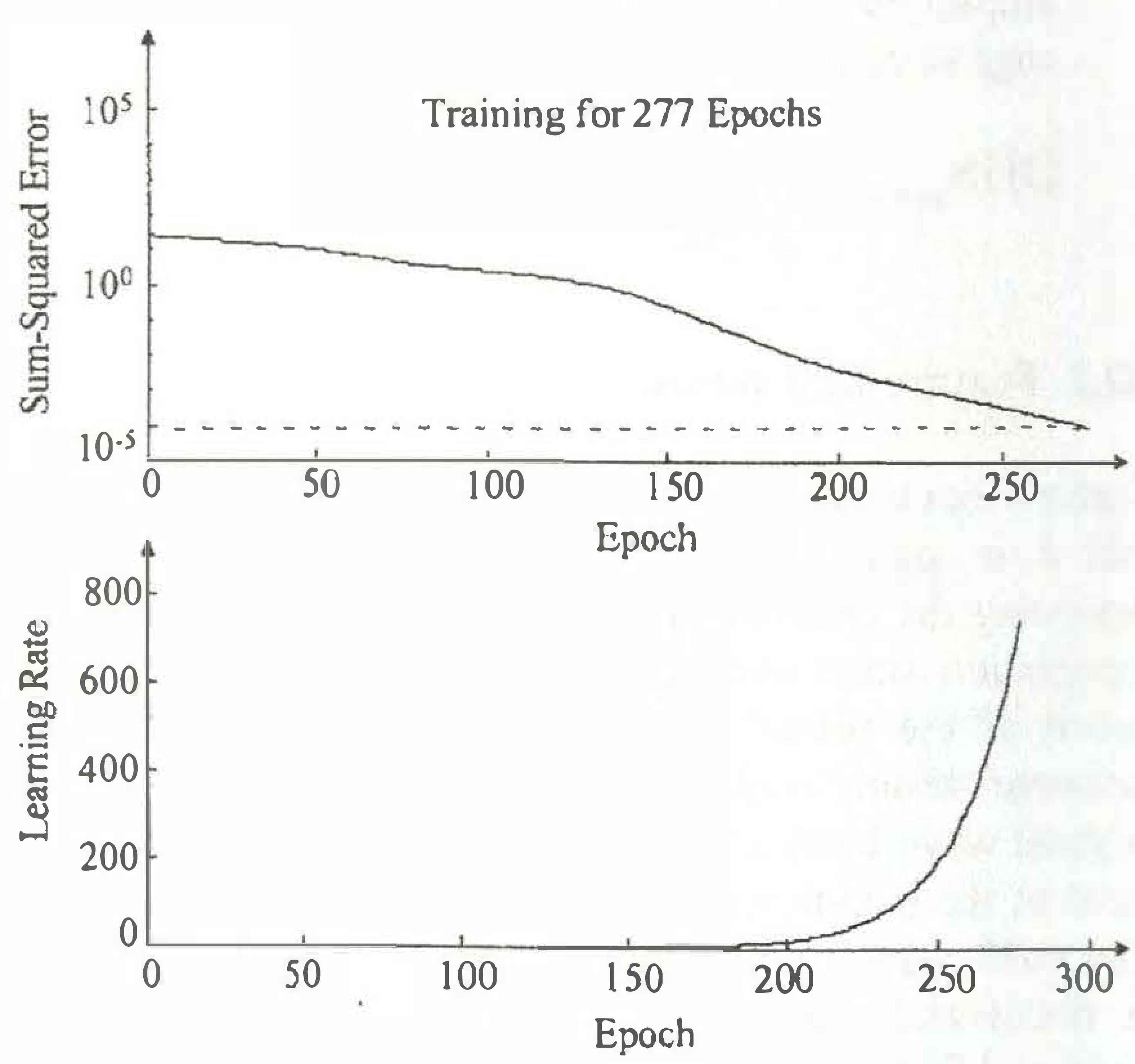

Fig. 8. The ANN training performance.

IV. EXPERIMENTAL RESULTS

We performed experiments using 215 heart aortic and mitral valve Doppler studies taken from different individuals. The data from a part of the DHS signal samples were used for training and another part in testing the ANN. In the experiments, 100 percent correct classification was obtained at the ANN training for the two signal classes. It clearly indicates the effectiveness and the reliability of the proposed approach for extracting features from DHS signals. The ANN testing results are tabulated in Table 2.

Table 2. Performance of the decision support system

	The heart aortic valve		The heart mitral valve	
	N	AN	N	AN
Total number of samples	31	40	19	33
Correct classification #	25	40	17	30
Incorrect classification #	5	---	2	3
The average recognition %	95.6	100	99.9	99.9
The highest recognition %	100	100	99.9	100
The lowest recognition %	74.4	100	99.9	99.9

N : Normal, AN: Abnormal

V. DISCUSSION AND CONCLUSION

In this study, we developed a decision support system for the interpretation of the DHS signals using pattern recognition and demonstrated the diagnosis performance of this method on the heart aortic and mitral valves. The task of feature extraction was performed using the wavelet decomposition for multi-scale analysis, PSD for time-frequency representations, and the wavelet entropy, while classification was carried out by the back-propagation neural network. The stated results show that the proposed method can make an efficient interpretation. Although for the abnormal subjects 95% correct classification were attained, the ratio was 84% for the normal subjects.

The feature choice was motivated by a realization that wavelet decomposition essentially is a representation of a signal at a variety of resolutions. In brief, the wavelet decomposition has been demonstrated to be an effective tool for extracting information from the DHS signals. Moreover, the proposed feature extraction method is robust against the noise in the DHS signals.

In this paper, the application of the wavelet entropy to the feature extraction from DHS signals was shown. Wavelet entropy proved to be a very useful tool for characterizing the DHS signal, furthermore the information obtained with the wavelet entropy probed not to be trivially related with the energy and consequently with the amplitude of signal. This means that with this method, new information can be accessed with an approach different from the traditional analysis of amplitude of DHS signal.

The most important aspect of the decision support system is the ability of self-organization of the neural network without requirements of programming and the immediate response of a trained net during real-time applications. These features make the decision support system suitable for automatic classification in interpretation of the DHS signals. These results point out the ability of design of a new intelligence diagnosis assistance system.

The diagnosis performances of this study show the advantages of this system: it is rapid, easy to operate, non-invasive, and not expensive. This system is of the better clinical application over others, especially for earlier survey of population. However, the position of the ultrasound probe, which is used for data acquisition from the heart valves, must be taken into consideration by physician.

Although our decision support system was carried out on the heart aortic and mitral valves, similar results for the other valves (tricuspid and pulmonary) and the other Doppler studies can be expected. Besides the feasibility of a real-time implementation of the decision support system, by increasing the variety and number of DHS signals additional information (i.e., quantification of the heart valve regurgitation and stenosis) can be provided for diagnosis.

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REFERENCES

[1] Akay, M., Akay Y.M., & Welkowitz, W. (1992). Neural networks for the diagnosis of coronary artery disease. *International Joint Conference on Neural Networks, IJCNN,* vol. 2, 419–424.

[2] Nanda, N.C. (1993). *Doppler Echocardiography.* Lea & Febiger, Second edition, London.

[3] Plett, M.I. (2000). *Ultrasonic arterial vibrometry with wavelet based detection and estimation.* University of Washington, Phd Thesis, 17-18.

[4] Philpot, E. F., Yoganathan, A.P., & Nanda, N.C. (1993). *Future Directions in Doppler Echocardiography.* Doppler Echocardiography, Lea & Febiger Philadelphia, London.

[5] Keeton, P.I.J., & Schlindwein, F.S. (1997). Application of wavelets in Doppler ultrasound. *MCB University Press*,Vol. 17, Number 1, 38--45.

[6] Wright, I.A., Gough, N.A.J., Rakebrandt, F., Wahab, & M., Woodcock J.P. (1997). Neural Network Analysis of Doppler Ultrasound Blood Flow Signals: A Pilot Study. *Ultrasound in Med. & Biol.*, vol. 23, No.5, 683-690.

[7] Jing, F., Xuemin, W., Mingshi, W., & Wie, L. (1997). Noninvasive Acoustical Analysis System of Coronary Heart Disease. *Biomedical Engineering Conference, Proceedings of the 1997 Sixteenth Southern*, 239 -241.

[8] Izzetoglu, K., Erkmen, A.M, & Beksac, S. (1995). Intelligent classification of fetal Doppler blood velocity waveform abnormalities using wavelet transform and vector quantization algoritlun. *IEEE International Conference on Systems, Man and Cybernetics, Intelligent Systems for the 21st Century*, vol.1, 724-729.

[9] Guler, I., & Kara, S. (1995). Detection of mitral stenosis by a pulsed Doppler flow meter and autoregressive spectral analysis method. *14th Conference of the Biomedical Engineering Society of India. An International Meeting, Proceedings of the First Regional Conference, IEEE*, 2/91 -2/92.

[10]Chan, B.C.B., Chan, F.H.Y., Lam, F.K., Lui, P.W., & Poon, P.W.F. (1997). Fast Detection of Venous Air Embolism is Doppler Heart Sound Using the Wavelet Transform. *IEEE Trans. on biomedical engineering*, vol. 44, no. 4, 237-245.

[11]Dickhous H., & Heinrich, H. (1996). Classifying Biosignals with Wavelet Networks. *IEEE Engineering in Medicine and Biology*, 103-111.

[12]Bishop, C.M. (1996). *Neural Networks for Pattern Recognition*. Clarendon Press, Oxford.

[13]Saini, V.D., Nanda N.C., & Maulik, D., (1993). *Basic Principles of Ultrasound and Doppler Effect.* Doppler Echocardiography, Lea & Febiger Philadelphia, London.

[14]Madeira, M.M., Tokhi, M.O., & Ruano, M. G. (2000). Real-time implementation of a Doppler signal spectral estimator using sequential and parallel processing techniques. *Elsevier Microprocessors and Microsystems*, vol.24, 153–167.

[15]Karabetsos, E., Papaodysseus, C., & Koutsouris, D. (1998). Design and development of a new ultrasonic doppler technique for estimation of the aggregation of red blood cells. *Elsevier Meas.*, vol.24, 207–215.

[16]Liang, H., & Nartimo, I. (1998). A feature extraction algorithm based on wavelet packet decomposition for heart sound signals. *Proceedings of the IEEE-SP International Symposium*, 93 -96.

[17]Akay, M. (1997). Wavelet applications in medicine. *IEEE Spectrum*, May 1997, vol. 34, 50 -56.

[18]Quiroga, R.Q. (1998). *Quantitative Analysis of EEG signals: Time-Frequency Methods and Chaos Theory.* Intitute of Physiology – Medical University Lübeck.

[19]Devasahayam, S.R. (2000). *Signals and Systems in Biomedical Engineering*. Kluwer Academic Publishers.

[20]Burrus, C.S., Gopinath, R.A., & Guo, H. (1998). *Introduction to Wavelet and Wavelet Transforms.* Prentice Hall, New Jersey, USA.

[21]Coifman, R.R., & Wickerhauser, M.V. (1992). Entropy-based Algorithms for best basis selection. *IEEE Trans. on Inf. Theory*, vol. 38, 2, 713-718.

[22]Quiroga, R.Q., Roso, O.A., & Basar, E. (1999). Wavelet entropy: a measure of order in evoked potentials. *Elsevier Science, Evoked Potentials and Magnetic Fields*, September, 49, 298-302.

[23]Haykin, S. (1994). *Neural networks, A Comprehensive Foundation.* Macmillan College Publishing Company Inc.,New York.

[24]Nichols, W.W., & O'Rourke, M.F. (1990). *McDonald's blood flow in arteries: Theoretical, experimental and clinical principles.* Arnold Publishers: New York, 3rd edition.

[25]Asres, A., Dou, H., Zhou, Z., Zhang, Y., & Zhu, S. (1997). A combination of AR and neural network technique for EMG pattern identification. *Engineering in Medicine and Biology Society, Bridging Disciplines for Biomedicine, 18th Annual International Conference of the IEEE*, vol.4, 1464 -1465.

[26]Allan, R., & Kinsner, W. (2001). A study of microscopic images of human breast disease using competitive neural networks. *Canadian Conference on Electrical and Computer Engineering*, vol.1, 289 -293.

[27]Brameier, M., & Banzhaf, W. (2001). A comparison of linear genetic programming and neural networks in medical data mining. *IEEE Transactions on Evolutionary Computation*, vol. 5, Feb 2001, 17-26.

[28]Miller, S., Bews, J., & Kinsner, W. (2001). Brachytherapy cancer treatment optimization using simulated annealing and artificial neural networks. *Canadian Conference on Electrical and Computer Eng.*, vol.1, 649–654.

[29]Turkoglu, I., & Arslan, A. (2001). An intelligent pattern recognition system based on neural network and wavelet decomposition for interpretation of heart sounds. *23rd Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, October 25-28 2001, pp.4.2.7-3, Istanbul, Turkey.

[30]Saraoğlu, H.M., Yumusak, N. & Ferikoğlu A., (1999). Training of Brain Signals by using Neural Networks. *International symposium on Mathematical & Computational Applications*, September 1-3, 1999, 249-254, Bakü, Azerbaijan.

[31]Bakhtazad, A., Palazoglu, A., & Romagnoli, J. A. (1999). Process data de-noising using wavelet transform. *Intelligent Data Analysis*, vol. 3, October 1999, 267-285.