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Automatic Continuous ECG Monitoring System for Over-drug Detection in Brugada Syndrome

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Abstract— **This paper is concerned with the automatic control of drug administration in patients suffering from Brugada Syndrome (BS). Drugs such as flecainide, procainamide, ajmaline and pilsicainide should be administrated under carefully controlled electrocardiogram (ECG) monitoring given that the treatment must be stopped if some ECG disturbing conditions appear. These conditions are, among others the development of premature ventricular contraction (PVC), atrial fibrillation (AF) and the widening of the QRS wave. The proposed system can detect these abnormalities by using a pattern recognition approach based on Hidden Markov Models (HMM) with features extracted from three scales of the Wavelet Transform (WT). Performances higher than 98% were reached regarding the classification of normal and abnormal pulses. The system was trained and tested mainly in data from the standard MIT-BIH arrhythmia database.**

I. Introduction

The Brugada syndrome has attracted great interest because of its high incidence in some parts of the world and its association with high risk for sudden death in young and healthy adults. Only automobile accidents cause more deaths than the BS in some countries [1].

While BS is associated with a peculiar pattern on ECG, automatic diagnosis is very difficult since other clinical criteria than the ECG pattern are required. Patients with typical ECG features but clinical criteria other than BS are said to have the Brugada pattern but not BS [2].

BS is associated with a persistent ST segment elevation in leads V1 to V3, although isolated cases have been described involving the inferior leads; such patients appear to have a unique mutation [3]. Three distinct types of ST segment elevation have been described. In type 1, the ST segment gradually descends to an inverted T wave. In type 2, the T wave is positive or biphasic, and the terminal portion of the ST segment is elevated more than 1 mm. In type 3, the T wave is positive, and the terminal portion of the ST segment is elevated less than 1 mm.

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Once detected BS, especially type 1 ECG pattern can occasionally be unmasked by sodium channel blockers (eg, flecainide, procainamide, ajmaline and pilsicainide) [1]. The reported sensitivity to these drugs has been variable, ranging from 100% [4] to as low as 15% [5]. The administration of these drugs takes about 10 minutes except ajmaline that takes about 5 minutes, and should be performed under continuous ECG monitoring [1]. Indications for termination are development of a diagnostic type 1 Brugada ECG, a ≥ 2 mm increase in ST segment elevation in patients with a type 2 Brugada ECG, the development of ventricular premature beats or other arrhythmias, or widening of the QRS $\geq 30\%$ above baseline [6].

This paper presents an automatic system that can detect some of the above abnormalities requiring termination of the drug administration process. Only PVCs, AF and QRS widening are considered in the ambit of this paper. The system is based on HMMs supported by wavelet based features.

HMMs have been successful applied to ECG segmentation and arrhythmia classification [7, 8] to name only a few, therefore they seem to be appropriate for the current purpose. Regarding HMM morphology a Bakis or left-to-right Continuous Density Hidden Markov Models (CDHMMs) with a Gaussian Mixture Model (GMM) associated to each model state transition was used. Although more complete HMMs structures have shown better performance especially for ECG synthesis purposes [12], simpler HMMs structures can capture most of the information regarding ECG pulse classification [8]. The ECG signal is previously sliced in singular pulses by using the Pan-Tompkins [9] algorithm and each pulse class is modeled by a six state model, modeling the Q-S, S-T, T, T-P, P and P-Q events. GMMs model a synthesized signal obtained from the inverse wavelet transform (IWT) of three selected scales of the WT. The Wavelet Transform (WT) has the advantage over conventional techniques that time/frequency representation can be more accurately modeled by decomposing the signal in the corresponding scales. When the composition level decreases in the time domain it increases in the frequency domain providing zooming capabilities and instantaneous characterization of the signal [10, 11].

The system presents Sensibility and positive Predictivity above 96% in the detection of PVC (V) and normal pulses (N) in the AF and VT rhythms, and RBBB (R) pulses in the normal rhythm (N). Additionally elongated QRS embedded in normal rhythm ECG pulses must also be detected. Regarding detection of normal and abnormal pulses, which is the goal in the present application, the performance rises

to more than 99%, reaching 100% considering that the 1% of pulses are not wrongly classified, instead they are separated for physician analysis given the uncertainty in the recognition engine. Only certainties above a predetermined threshold were effectively considered.

Training and testing data for ventricular and atrial arrhythmias are from MIT-BIH database. QRS wide examples were artificially generated from normal pulses and regarding the test phase this measure is obtained by backtracking the most likely state sequence in the Viterbi algorithm.

II. Wavelets Analysis of ECG

The wavelet transform (WT) is a signal representation in a scale-time space, where each scale represents a focus level of the signal and therefore can be seen as a result of a band-pass filtering.

The most usual way to sample the time-scale plane is on a so-called "dyadic" grid, which means that sampled points in the time-scale plane are separated by a power of two.

As the scale represents the level of focus from the which the signal is viewed and which is related to the frequency range involved, then digital filter banks are appropriate to break the signal into different scales (bands). If the progression in the scale is "dyadic" the signal can be sequentially half-band high-pass and low-pass filtered.

The output of the high-pass filter represents the detail of the signal. The output of the low-pass filter represents the approximation of the signal, for each decomposition level, and will be decomposed in its detail and approximation components at the next decomposition level, and the process proceeds iteratively in a scheme known as wavelet decomposition tree, which is shown in figure 1. After the filtering half of the samples can be eliminated according to the Nyquist's rule, since the signal now has only half of the frequency.

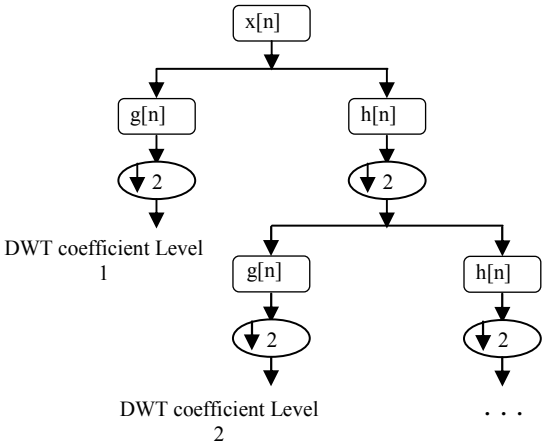

Figure 1 Wavelet decomposition tree

This very practical filtering algorithm yields as Fast Wavelet Transform (FWT) and is known in the signal processing community as two-channel subband coder [10].

One important property of the Discrete Wavelet Transform (DWT) is the relationship between the impulse responses of the high-pass (g[n]) and low-pass (h[n]) filters, which are not independent of each other and they are related by

$$g[L-1-n] = (-1)^n h[n] \quad (1)$$

where L is the filter length in number of points. Since the two filters are odd index alternated reversed versions of each other they are known as Quadrature Mirror Filters (QMF). Perfect reconstruction requires, in principle, ideal half-band filtering. Although it is not possible to realize ideal filters, under certain conditions it is possible to find filters that provide perfect reconstruction. The most famous ones were developed by Ingrid Daubechies and they are known as Daubechies wavelets. In the ambit of this work only the three least scales of Daubechies wavelets with 2 vanishing moments (db-4) were used. No other wavelet types were tried since this topic is out of the scope of this paper.

The multiresolution analysis based on the DWT can enhance small differences when the signal is simultaneously observed at the most appropriate scales. Figure 2 shows the result of the application of the DWT one cycle of a normal ECG.

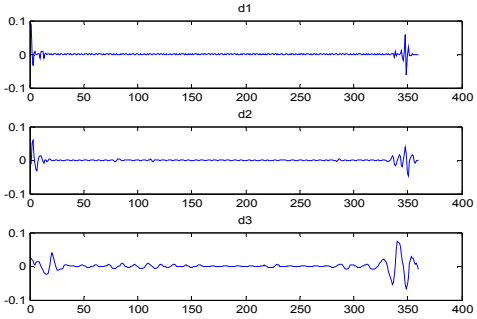

Figure 2 One ECG pulse viewed at scales d1, d2 and d3

From the figure we can observe that d1 level (frequency ranges of 90-180Hz) emphasize the high frequency content of complex QRS when compared with P and T waves. D2 and d3 levels show clearly that other waves of small frequencies not seen at d1 scale are just appearing.

The features used in the scope of this work are simultaneous observations of d1, d2 and d3 scales, therefore the observation sequence generated after the parameter extraction is of the form $\mathbf{O}=(\mathbf{o}_1, \mathbf{o}_2, \ldots \mathbf{o}_T)$ where T is the signal length in number of samples and each observation $\mathbf{o}_t$ is a tri-dimensional vector. Each element of the observation vector is derived from the Inverse Wavelet Transform (IWT) of the selected scale.

III. HIDDEN MARKOV MODELS

Hidden Markov models are a doubly stochastic process in which the observed data are viewed as the result of having passed the hidden finite process (state sequence) through a function that produces the observed (second) process.

In the pattern recognition paradigm each class of beat is represented by a separate model and after decoding, the class for which the probability (likelihood) of occurrence is greater is selected. Since the ECG is characterized by a time sequence waves occurring almost always in the same order which reflects the sequential activity of the cardiac conduction system an HMM structure where the states are connected in a left-to-right order was adopted. In [12] it is shown that a full connected HMM is eventually more appropriate for HMM modeling since the beat sequence reproduced by this kind of HMM is almost perfect. Figure 3 shows the model structure adopted for the several pathologies considered in the ambit of this paper.

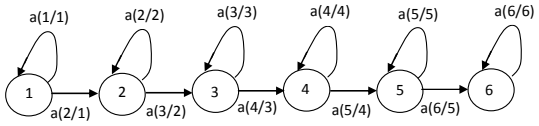

Figure 3 A left-to-right HMM with 6 states

The next issue is the choice of the number of Gaussian mixtures. For continuous models (CDHMMs), it has been found that it is more convenient and sometimes preferable to use diagonal covariance matrices with several mixtures, rather than fewer mixtures with full covariance matrices. The reason is the difficulty in performing reliable re-estimation of the off diagonal components of the covariance matrix from the necessarily limited training data. The HMMs in this work use five Gaussian mixtures per transition.

The output probability density function, which defines the conditional likelihood of observing a set of features when a transition through the model takes place, is usually a multivariate Gaussian mixture for the most engineering applications involving hidden Markov models. These probability density functions are associated with the transitions which configures a Continuous Density Hidden Markov Models (CDHMMs) Mealy machine and are given by

$$f(y/u_t) = \sum_{i=1}^{C} b_{u_t,i} G(y_t, \mu_{u_t,i}, \Sigma_{u_t,i}) \tag{2}$$

where c is the number of components in the Gaussian mixture, G(…) stands for bi-variate normal distribution with mean vector and covariance matrix for the i[th] mixture component and transition u_t given respectively by $\mu_{u_t,i}$ and $\Sigma_{u_t,i}$. As the components of observation vector are assumed iid G(…) function in equation (2) is simply the product of five Gaussian functions. The mixture coefficients $b_{u_t,i}$ satisfy, for each transition u_t, to

$$\sum_{i=1}^{C} b_{u_t,i} = 1 \tag{3}$$

so that, equation (2) is a probability density function. In our experiments the observations were modeled by five components in the Gaussian mixture (C=5) in order to fit best the data with multimodal distributions.

The Estimation of HMM parameters from a set of representative training data can be done by using the Baum-Welch algorithm which is based on the decoding of all the possible state sequence, or alternatively by using the Viterbi algorithm which is based on the most likely state sequence [13]. The adopted training was the MLE procedure in the Viterbi framework, which goal is to maximize iteratively the following probability density function

$$f(Y/\lambda) = f(Y/S,\lambda)P(S/\lambda) \tag{4}$$

where Y is the observation sequence, S the most likely state sequence and λ the set of HMM parameters. The model reestimation formulas can be found in [13].

IV. EXPERIMENTAL RESULTS

Experimental results were evaluated by using the MIT-BIH Arrhythmia Database and also some records belonging to our medical staff labeled as 300 and 301. Normal (N), premature ventricular contraction (V) and right bundle branch block (R), in atrial fibrillation (AF), ventricular bigeminy (B), normal (N) and ventricular tachycardia (VT) rhythms were selected. QRS wide examples were artificially generated from normal pulses of normal rhythm. A controlled interpolation followed by low-pass filtering was used for this purpose.

The training set contains the 106, 118, 121, 122 and 221 records and the testing set contains the 105, 106, 112, 118, 121, 122, 205, 210, 221 records of the MIT-BIH arrhythmia database, 300 and 301 of the Data-Acquisition System. For the training set 1445 normal (N) pulses of 121 (N rhythm) and 122 (N rhythm), 682 normal and premature ventricular contraction (V) pulses of 221 (AF rhythm), 162 premature ventricular contraction of 106 (B and VT (V rhythm)) and 187 right bundle branch block (R) pulses of 118 (N rhythm) records were used. The testing set contains 3432 pulses of 105, 106, 112, 121, 122, 205, 300 and 301 records, 1011 pulses of 210 and 221 records and 412 pulses of 118 records, which means that data for training and testing purposes was

obtained from different patients, which is normally known as patient-independent analysis. The variance of the performance was not tested for other combinations of the training and testing set since the first goal is to evaluate the effectiveness of the system on testing data from real patients, so not belonging to the MIT-BIH database. Table 1 shows the HMM based pulse classification system using features from wavelets selected from IWT at three different scales, respectively d1, d2 and d3. Both MLII and V1 signals were used with their own HMM. A pulse is considered classified if the score from both models agree, otherwise the pulse is considered wrong. Wrong pulses are separated for posterior analysis by the physician while the misclassified pulses shown in Table 1 are derived from classified pulses.

The row labeled "Total" means the total number of beats used in experiment for each class listed in the corresponding column.

Regarding QRS wide detection only normal pulses of normal rhythm were tested since other rhythms than normal do not occur in the ambit of the current application, which stops under abnormal rhythm conditions. This measure is obtained by backtracking the most likely state sequence in the Viterbi algorithm.

TABLE 1
THE CONFUSION MATRIX

	AFN	AFV	NN	NR	VV	Total	Pr+
AFN	864	0	0	0	0	864	1
AFV	0	114	0	0	0	114	1
NN	33	0	3391	5	0	3429	0.98
NR	0	0	0	407	0	407	1
VV	0	0	0	0	41	41	1
Total	897	114	3391	412	41	4855	
Sensitivity	0.96	1	1	0.98	1		

The QRS wide baseline is set to the average of all QRS wide before drug administration starts. After starting the drug administration all normal pulses in the normal rhythm are submitted to the QRS wide measure. Measures ≥ 1.3 baselines originate a system alarm, as well as detection of any arrhythmia.

V. CONCLUSION

This paper reports a robust ECG classification system, regarding cardiac arrhythmia detection, with applications in the administration drug control in patients suffering from Brugada Syndrome. The current system does not detect yet 2 indications that must stop de drug administration, namely the diagnostic type 1 Brugada and a 2mm increase in ST segment elevation in patients with a type 2 Brugada. This topic is currently under research. Only pulses classified in the same class for both derivations were considered correctly classified pulses. Pulses classified in different classes in each derivation are uncertainty pulses selected for posteriori physician analysis. This procedure improves the true positive rate requiring however physician intervention for reliable diagnosis requirements. This system takes advantage of advanced signal processing techniques as WT and HMM's. WT allows observing the signal at different scales, each one emphasizing some signal properties and characteristics. By using simultaneously different scales more signal properties can be simultaneously observed hence better characterized will be the ECG pulse. As a matter of fact, different and opposite properties as the low content frequency of the P-wave and the high content frequency of the QRS can be accurately simultaneously observed. HMM's are statistical models adequate for modeling signals of non-stationary nature. Assuming that WT can emphasize the non-stationary of the ECG by emphasizing their frequency content that varies with time, then HMM's appear as a natural model with recognized capacities to break the ECG in quasi-stationary segments. Hence both techniques can complement each other in the analysis of signals of non-stationary nature.

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