Coronary Damage Classification of Patients with the Chagas Disease with Error-Correcting Output Codes

Sergio Escalera, Oriol Pujol, Eric Laciar, Jordi Vitrià, Esther Pueyo, and Petia Radeva

Abstract— The Chagas' disease is endemic in all Latin America, affecting millions of people in the continent. In order to diagnose and treat the chagas' disease, it is important to detect and measure the coronary damage of the patient. In this paper, we analyze and categorize patients into different groups based on the coronary damage produced by the disease. Based on the features of the heart cycle extracted using high resolution ECG, a multi-class scheme of Error-Correcting Output Codes (ECOC) is formulated and successfully applied. The results show that the proposed scheme obtains significant performance improvements compared to previous works and state-of-the-art ECOC designs.

Index Terms— Chagas disease, Error-Correcting Output Codes, high resolution ECG, decoding

I. Introduction

Chagas' disease is an infectious illness caused by the parasite Tripanosoma Cruzi, which is transmitted to humans through the feces of a bug called Triatoma infestans. The World Health Organization (WHO) estimates that 16 to 18 million people in Latin American countries are already infected by the disease and other 100 million people are at risk of being infected [19].

In general terms, two different stages of Chagas' disease can be distinguished. The first stage, called acute phase, appears shortly after the parasitical infection and it is occasionally manifested by high temperature, inflammations, and heart rate acceleration. Following this phase, which lasts for one or two months, there is an undetermined latent period. After that, some patients go into a chronic phase, which is characterized by alterations in the cardiovascular system, normally associated to the so-called Chagas' cardiomyopathy. This type of cardiomyopathy produces malfunctioning in the propagation of the electrical impulse as well as destruction of cardiac fibers. In areas where the illness is endemic, Chagas' cardiomyopathy represents the first cause of cardiovascular death [16].

In order to optimize treatment for chronic chagasic patients, it is essential to make use of an effective diagnosis tool able to determine the existence of cardiac injury and, if positive, its magnitude. Clinical diagnosis is usually based on tests such as chest x-rays, echocardiogram, or electrocardiogram (ECG), which can be either Holter ECG or conventional rest ECG. The use of high-resolution electrocardiography (HRECG) has been reported in the literature as a useful tool for clinical assessment of Chagas' disease [3][6][18]. Specifically, the presence of ventricular late

potentials (VLP) has been detected in chronic chagasic patients using high-resolution ECGs. VLP, which are usually measured on temporally averaged beats, are very low-amplitude high-frequency signals found within the terminal part of the QRS complex and the beginning of the ST segment. A different approach has been proposed in other studies [14][15], in which the beat-to-beat variability of the QRS duration on HRECG has been measured, and it has been shown that such a variability is more accentuated in chagasic patients, particularly when the degree of myocardial damage is severe.

Since Chagas' cardiomyopathy frequently leads to alterations in the heart's electrical conduction, recently it has been proposed the slopes of QRS complex in order to determine the myocardial damage associated with the disease [22]. Based on the temporal indices and slopes of QRS complex as extracted features, an automatic system that categorized patients into different groups is presented. To perform a multi-classification system able to learn the level of damage produced by the disease, we focus on Error-Correcting Output Codes. ECOC were born as a general framework to combine binary problems to address the multi-class problem [5]. Based on the error correcting principles and because of its ability to correct the bias and variance errors of the base classifiers [13], ECOC has been successfully applied to a wide range of Computer Vision applications, such as face recognition [27], face verification [12], text recognition [10] or manuscript digit classification [29].

The ECOC technique can be broken down into two distinct stages: encoding and decoding. Given a set of classes, the coding stage designs a codeword[1] for each class based on different binary problems. The decoding stage makes a classification decision for a given test sample based on the value of the output code.

Many coding designs have been proposed to codify an ECOC coding matrix, obtaining successful results [7][24]. However, the use of a proper decoding strategy is still an open issue. In this paper, we propose the Loss-Weighted decoding strategy, witch exploits the information provided at the coding stage to perform a successful classification. As a result, our system automatically diagnoses the level of coronary damage of patients with the Chagas' disease. The results show that the present ECOC scheme outperforms the state-of-the-art on decoding designs, at same time that obtains significant performance improvements characterizing the level of damage of patients with the Chagas' disease.

The paper is organized as follows: Section 2 explains the feature extraction from QRS complex of chronic chagasic patients. Section 3 presents the Loss-Weighted decoding strategy to decode any ECOC design. Section 4 shows the experimental results of the multi-class categorization system, and finally. Finally, section 5 concludes the paper.

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[1]The codeword is a sequence of bits of a code representing each class, where each bit identifies the membership of the class for a given binary classifier.

II. QRS FEATURES

To obtain the features to evaluate the degree of myocardial damage associated with the disease, the QRS slopes are analyzed for all the HRECG recordings of 107 individuals from the Chagas database recorded at Simón Bolívar University (Venezuela). For each recording, let's denote $x_i(n), n = 0, ..., N$, the i-th beat of lead X, where i runs from 0 to I (being I the total number of beats in the recording). Analogously, let's denote $y_i(n)$ and $x_i(n)$ the i-th beats of leads Y and Z, respectively. QRS slopes are measured on temporally averaged signals $\overline{x}(n)$, $\overline{y}(n)$, and $\overline{z}(n)$, $n = 0, ..., N$, which are calculated as the average of all normal beats $i = 0, ..., I$ of the recording. Ectopic and grossly noisy beats were excluded of the averaging process. The averaging is performed following the standard recommendations described in [2].

A three-step process is applied to compute the upward QRS slope, α_{US}, and the downward QRS slope, α_{DS}, of each averaged beat $\overline{x}(n)$, $\overline{y}(n)$, and $\overline{z}(n)$. In the first step, delineation is performed using a wavelet-based technique [17] that determines the temporal locations Q, R, and S wave peaks, which are denoted by n_Q, n_R, and n_S, respectively [23]. The second step identifies the time instant n_U associated with maximum slope of the ECG signal (i.e., global maximum of its derivative) between n_Q and n_R. Analogously, the time instant n_D corresponding to minimum slope of the ECG signal between n_R and n_S is identified. As a final step, a line is fitted in the least squares sense to the ECG signal in a window of 15ms around n_U, and the slope of that line is defined as α_{US}. In the same manner, α_{DS} is defined as the slope of a line fitted in a 15ms window around n_D.

Other temporal indices defined to detect the presence of VLP in HRECG recordings are also evaluated in this work. Previous studies in the literature have shown the ability of those indices to determine the severity of Chagas' cardiomyopathy [14][15]. Consequently, we use such indices in conjunction with the QRS slopes. Computation of QRS-based indices considers filtered leads X, Y, and Z using a bi-directional 4th-order Butterworth filter with passband between 40 and 250 Hz. The filtered signals are denoted by $x_{i,f}(n)$, $y_{i,f}(n)$, and $z_{i,f}(n)$.

The QRS-based indices $QRSD$, $RMS40$, and $LAS40$, which are described next, require temporal signal averaging ($\overline{x_f}(n)$, $\overline{y_f}(n)$, and $\overline{z_f}(n)$) as well as the calculation of the vector magnitude, defined as follows:

$$v(n) = \sqrt{\overline{x_f}^2(n) + \overline{y_f}^2(n) + \overline{z_f}^2(n)} \tag{1}$$

On the signal $v(n)$ the three temporal QRS indices defined to detect VLP are computed based on identification of time instants n_b and n_e corresponding to the beginning and the end of the QRS complex [2]:

$$QRSD = n_e - n_b \tag{2}$$

$$RMS40 = \sqrt{\frac{1}{n_2 - n_1} \sum_{n=n_1}^{n_2} v^2(n)}, n_1 = n_e - 40ms, n_2 = n_e \tag{3}$$

$$LAS40 = n_e - argmax\{n|v(n) \geq 40\mu V\} \tag{4}$$

On the other hand, the index $\Delta QRSD$ is considered, which is defined next. This index is measured on the vector magnitude of the ultraveraged filtered leads ($x_{i,f}(n)$, $y_{i,f}(n)$, $z_{i,f}(n)$):

$$v_i(n) = \sqrt{x_{i,f}^2(n) + y_{i,f}^2(n) + z_{i,f}^2(n)} \tag{5}$$

On each signal $v_i(n)$, $i = 0, .., I$, the duration of its complex QRS is estimated and denoted by $QRSD_i$. The index $\Delta QRSD$ is defined as the standard deviation of the beat-to-beat $QRSD_i$ series [15]:

$$\Delta QRSD = \sqrt{\frac{\sum_{i=1}^{I}(QRSD_i - \overline{QRSD}^2)}{I-1}}$$
$$\overline{QRSD} = \frac{\sum_{i=1}^{I} QRSD_i}{I} \tag{6}$$

Based on the previous features, we present a design of Error-Correcting Output Codes that automatically diagnoses the level of damage of patients with the Chaga's disease.

III. ERROR-CORRECTING OUTPUT CODES

Given a set of N_c classes to be learned, at the coding step of the ECOC framework, n different bi-partitions (groups of classes) are formed, and n binary problems (dichotomies) are trained. As a result, a codeword of length n is obtained for each class, where each bin of the code corresponds to a response of a given dichotomy. Arranging the codewords as rows of a matrix, we define a "coding matrix" M, where $M \in \{-1, 0, 1\}^{N_c \times n}$ in the ternary case. Joining classes in sets, each dichotomy, that defined a partition of classes, codes by $\{+1, -1\}$ according to their class set membership, or 0 if the class is not considered by the dichotomy. In fig.1 we show an example of a ternary matrix M. The matrix is coded using 7 dichotomies $\{h_1, ..., h_7\}$ for a four class problem (c_1, c_2, c_3, and c_4). The white regions are coded by 1 (considered as positive for its respective dichotomy, h_i), the dark regions by -1 (considered as negative), and the grey regions correspond to the zero symbol (not considered classes by the current dichotomy). For example, the first classifier (h_1) is trained to discriminate c_3 versus c_1 and c_2 ignoring c_1, the second one classifies c_2 versus c_1, c_3 and c_4, and so on.

During the decoding process, applying the n trained binary classifiers, a code x is obtained for each data point in the test set. This code is compared to the base codewords of each class $\{y_1, ..., y_4\}$ defined in the matrix M, and the data point is assigned to the class with the "closest" codeword [1][28].
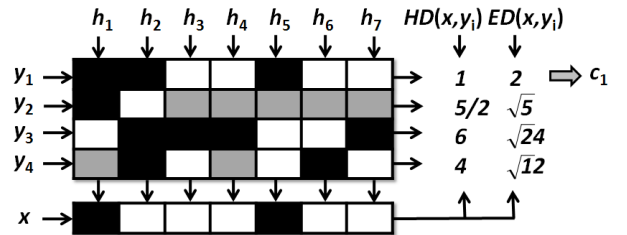

Fig. 1. Example of ternary matrix M for a 4-class problem. A new test codeword is classified by class c_1 when using the traditional Hamming and Euclidean decoding strategies.

A. Decoding designs

The decoding step decides the final category of an input test by comparing the codewords. In this way, a robust decoding strategy is required to obtain accurate results. Several techniques for the binary decoding step have been proposed in the literature [28][11][21][4], the most common ones are the Hamming (HD) and the Euclidean (ED) approaches [28]. In fig.1, a new test input x is evaluated by all the classifiers and the method assigns

label c_1 with the closest decoding distances. Note that in the particular example of fig. 1 both distances agree. In the work of [24], authors showed that the Euclidean distance was usually more suitable than the traditional Hamming distance in both the binary and the ternary cases. Nevertheless, little attention has been paid to the ternary decoding approaches.

In [1], the authors propose a Loss-based technique when a confidence on the classifier output is available. For each row of M and each data sample $\wp$, the authors compute the similarity between $f^j(\wp)$ and $M(i,j)$, where f^j is the jth dichotomy of the set of hypothesis F, considering a loss estimation on their scalar product, as follows:

$$D(\wp, y_i) = \sum_{j=1}^{n} L(M(i,j) \cdot f^j(\wp)) \quad (7)$$

where L is a loss function that depends on the nature of the binary classifier. The most common loss functions are the linear and the exponential one. The final decision is achieved by assigning a label to example $\wp$ according to the class c_i with the minimal distance.

Recently, the authors of [21] proposed a probabilistic decoding strategy based on the margin of the output of the classifier to deal with the ternary decoding. The decoding measure is given by:

$$D(y_i, F) = -log \left(\prod_{j \in [1,n]: M(i,j) \neq 0} P(x^j = M(i,j)|f^j) + \alpha \right) \quad (8)$$

where α is a constant factor that collects the probability mass dispersed on the invalid codes, and the probability $P(x^j = M(i,j)|f^j)$ is estimated by means of:

$$P(x^j = y_i^j|f^j) = \frac{1}{1 + exp(y_i^j(A^j f^j + B^j))} \quad (9)$$

Vectors A and B are obtained by solving an optimization problem [21].

IV. LOSS-WEIGHTED DECODING (LW)

In this section, we present the multi-class scheme of Error-Correcting Output Codes proposed to learn the QRS complex features described in section 2.

The ternary symbol-base ECOC allows to increase the number of bi-partitions of classes (thus, the number of possible binary classifiers) to be considered, resulting in a higher number of binary problems to be learned. However, the effect of the ternary symbol is still an open issue. Since a zero symbol means that the corresponding classifier is not trained on a certain class, to consider the "decision" of this classifier on those zero coded position does not make sense. Moreover, the response of the classifier on a test sample will always be different to 0, so it will register an error. Let return to fig. 1, where an example about the effect of the 0 symbol is shown. The classification result using the Hamming distance as well as the Euclidean distance is class c_1. On the other hand, class c_2 has only coded first both positions, thus it is the only information provided about class c_2. The first two coded locations of the test codeword x correspond exactly to these positions. Note that each position of the codeword coded by 0 means that both -1 and +1 values are possible. Hence the correct classification should be class c_2 instead of c_1. The use of standard decoding techniques that do not consider the effect of the third

symbol (zero) frequently fails. In the figure, the HD and ED strategies accumulate an error value proportional to the number of zero symbols by row, and finally miss-classify the sample x.

Given a coding matrix M,

1) Calculate the matrix of hypothesis H:

$$H(i,j) = \frac{1}{m_i} \sum_{k=1}^{m_i} \gamma(h_j(\wp_k^i), i, j) \quad (10)$$

based on $\quad \gamma(x_j, i, j) = \begin{array}{ll} 1, & \text{if} \quad x_j = M(i,j) \\ 0, & \text{otherwise.} \end{array} \quad (11)$

2) Normalize H so that $\sum_{j=1}^{n} M_W(i,j) = 1, \forall i = 1, ..., N_c$:

$$M_W(i,j) = \frac{H(i,j)}{\sum_{j=1}^{n} H(i,j)},$$
$$\forall i \in [1, ..., N_c], \quad \forall j \in [1, ..., n]$$

Given a test input $\wp$, decode based on:

$$d(\wp, i) = \sum_{j=1}^{n} M_W(i,j) L(M(i,j) \cdot f(\wp, j)) \quad (12)$$

TABLE I
LOSS-WEIGHTED ALGORITHM.

To solve the commented problems, we propose a Loss-Weighted decoding. The main objective is to find a weighting matrix M_W that weights a loss function to adjust the decisions of the classifiers, either in the binary and in the ternary ECOC frameworks. To obtain the weighting matrix M_W, we assign to each position (i,j) of the matrix of hypothesis H a continuous value that corresponds to the accuracy of the dichotomy h_j classifying the samples of class i (10). We make H to have zero probability at those positions corresponding to unconsidered classes (11), since these positions do not have representative information. The next step is to normalize each row of the matrix H so that M_W can be considered as a discrete probability density function (12). This step is very important since we assume that the probability of considering each class for the final classification is the same (independently of number of zero symbols) in the case of not having *a priori* information ($P(c_1) = ... = P(c_{N_c})$). In fig. 2 a weighting matrix M_W for a 3-class problem with four hypothesis is estimated. Figure 2(a) shows the coding matrix M. The matrix H of fig. 2(b) represents the accuracy of the hypothesis classifying the instances of the training set. The normalization of H results in the weighting matrix M_W of fig. 2(c)[2].

The Loss-weighted algorithm is shown in table I. As commented before, the loss functions applied in equation (12) can be the linear or the exponential ones. The linear function is defined by $L(\theta) = \theta$, and the exponential loss function by $L(\theta) = e^{-\theta}$, where in our case θ corresponds to $M(i,j) \cdot f^j(\wp)$. Function

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[2]Note that the presented Weighting Matrix M_W can also be applied over any decoding strategy.

$$M = \begin{bmatrix} 1 & 1 & \text{-}1 & 0 \\ 1 & \text{-}1 & 0 & 0 \\ 1 & 1 & 1 & \text{-}1 \end{bmatrix} \quad H = \begin{bmatrix} 0.955 & 0.955 & 1.000 & 0.000 \\ 0.900 & 0.800 & 0.000 & 0.000 \\ 1.000 & 0.905 & 0.805 & 0.805 \end{bmatrix}$$

(a) (b)

$$M_W = \begin{bmatrix} 0.328 & 0.328 & 0.344 & 0.000 \\ 0.529 & 0.471 & 0.000 & 0.000 \\ 0.285 & 0.257 & 0.229 & 0.229 \end{bmatrix}$$

(c)

Fig. 2. (a) Coding matrix M of four hypotheses for a 3-class problem. (b) Matrix H of hypothesis accuracy. (c) Weighting matrix M_W.

$f^j(\wp)$ may return either the binary label or the confidence value of applying the jth ECOC classifier to the sample $\wp$.

V. RESULTS

Before the experimental results are presented, we comment the data, methods, and evaluation measurements.

● *Data*: In this work, we analyzed a population composed of 107 individuals from the Chagas database recorded at Simón Bolívar University (Venezuela). For each individual, a continuous 10-minute HRECG was recorded using orthogonal XYZ lead configuration. All the recordings were digitalized with a sampling frequency of 1 kHz and amplitude resolution of 16 bits.

Out of the total 107 individuals of the study population, 96 are chagasic patients with positive serology for Trypanosoma Crucy, clinically classified into three different groups according on their degree of cardiac damage (Groups I, II, and III). This grouping is based on the clinical history, Machado-Guerreiro test, conventional ECG of twelve derivations, Holter ECG of 24 hours, and myocardiograph study for each patient. The other 11 individuals are healthy subjects with negative serology taken as a control group (Group 0). All individuals of the database are described with a features vector of 16 features based on the previous analysis of section 2. The four analyzed groups are described in detail next:

● Group 0: 11 healthy subjects in the age 33.6±10.9 years, 9 men and 2 women.

● Group I: 41 total patients with the Chagas' disease in the age of 41.4±8.1 years, 21 men and 20 women, but without evidences of cardiac damage in cardiographic study.

● Group II: 39 total patients with the Chagas' disease in the age of 45.8±8.8 years, 19 men and 20 women, with normal cardiographic study and some evidences of weak or moderate cardiac damage registered in the conventional ECG or in the Holter ECG of 24 hours.

● Group III: 16 total patients with the Chagas' disease in the age of 53.6±9.3 years, 9 men and 7 women, with significant evidences of cardiac damage detected in the conventional ECG, premature ventricular contractions and/or cases of ventricular tachycardiac registered in the Holter ECG and reduced fraction of ejection estimated in the cardiographic study.

● *Methods*: We compare our results with the performances reported in [22] for the same data. Moreover, we compare different ECOC designs: the one-versus-one ECOC coding strategy [25] applied with the Hamming [5], Euclidean [7], Probabilistic [21], and the presented Loss-Weighted decoding strategies. We selected the one-versus-one ECOC coding strategy because the individual classifiers are usually smaller in size than they would

be in the rest of ECOC approaches, and the problems to be learned are usually easier, since the classes have less overlap. Each ECOC configuration is evaluated for three different base classifiers: Fisher Linear Discriminant Analysis (*FLDA*) with a previous 99.9% of Principal Components [8], Discrete Adaboost with 50 runs of Decision Stumps [9], and Linear Support Vector Machines with the regularization parameter C set to 1 [26][20].

● *Evaluation measurements*: To evaluate the methodology we apply leave-one-patient-out classification on the Chagas data set.

A. Chagas data set categorization

We divide the Chagas categorization problem into two experiments. First, we classify the features obtained from the 107 patients considering the four groups in a leave-one-patient-out experiment for the different ECOC configurations and base classifiers. Since each patient is described with a vector of 16 features, 107 tests are performed. And second, the same experiment is evaluated over the 96 patients with the Chagas' disease from groups I, II, and III. This second experiment is more useful in practice since the splitting of healthy people from the patients with the Chagas' disease is solved with an accuracy upon 99.8% using the Machado-Guerreiro test.

1) 4-class characterization: The results of categorization for the four groups of patients reported by [22] are shown in fig. 3. Considering the number of patients from each group, the mean classification accuracy of [22] is of 57%. The results using the different ECOC configurations for the same four groups are shown in fig. 4. In fig. 4(a), the mean accuracy for each base classifier and decoding strategy is shown. The individual performances of each group of patients for each base classifier are shown in fig. 4(b), fig. 4(c), and fig. 4(d), respectively. Observing the mean results of fig. 4(a), one can see that any ECOC configuration outperforms the results reported by [22]. Moreover, even if we use *FLDA*, Discrete Adaboost, or Linear *SVM* in the one-versus-one ECOC design, the best performance is always obtained with the proposed Loss-Weighted decoding strategy. In particular, the one-versus-one ECOC coding with Discrete Adaboost as the base classifier and Loss-Weighted decoding attains the best performance, with a classification accuracy upon 60% considering the four groups of patients.
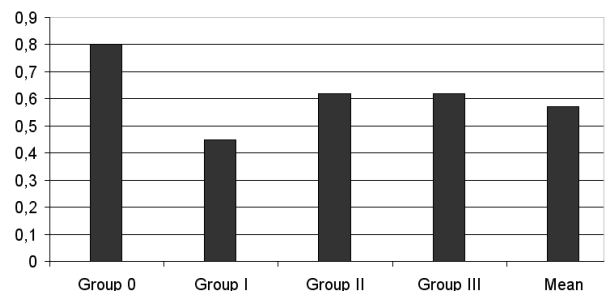

Fig. 3. Classification performance reported by [22] for the four groups of patients.

2) 3-class characterization: Now, we evaluate the same strategies on the three groups of patients with the Chagas' disease, without considering the healthy people. The new results are shown in fig. 5. In fig. 5(a), the mean accuracy for each base classifier and decoding strategy is shown. The individual performances of each group of patients for each base classifier are shown in fig. 5(b),

(a) Mean classification performance for each base classifier

(b) Classification performance for each group using *FLDA*

(c) Classification performance for each group using Discrete Adaboost

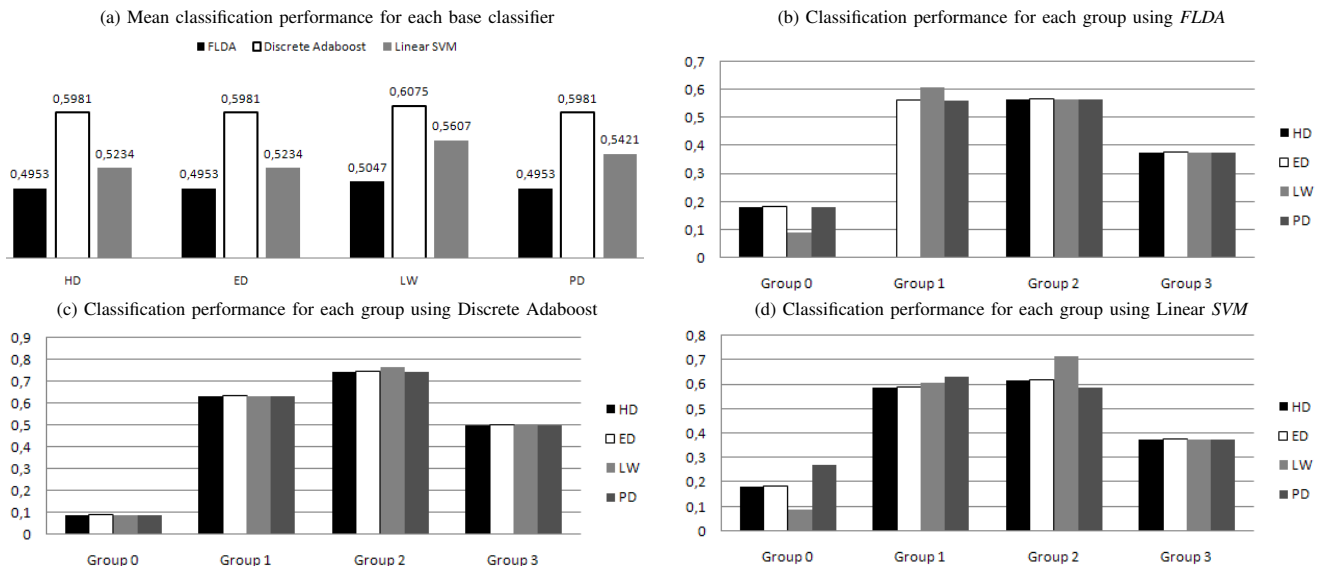(d) Classification performance for each group using Linear *SVM*

Fig. 4. Leave-one-patient-out classification using one-versus-one ECOC design (HD: Hamming decoding, ED: Euclidean decoding, LW: Loss-Weighted decoding, PD: Probabilistic decoding) for the four groups with and without Chagas' disease.

fig. 5(c), and fig. 5(d), respectively. In the mean results of fig. 5(a), one can see that independently of the base classifier applied, the Loss-Weighted decoding strategy attains the best performances. In this example, the one-versus-one ECOC coding with Discrete Adaboost as the base classifier and Loss-Weighted decoding also attains the best results, with a classification accuracy about 72% distinguishing among three levels of patients with the Chagas' disease.

VI. CONCLUSIONS

In this paper, we characterized patients with the Chagas' disease based on the coronary damage produced by the disease. We used the features extracted using the ECG of high resolution from the heart cycle of 107 patients, and presented a decoding strategy of Error-Correcting Output Codes lo learn a multi-class system. The results show that the proposed scheme outperforms previous works characterizing patients with different coronary damage produced by the Chagas' disease (upon 10% performance improvements), at the same time that it achieves better results compared with the state-of-the-art ECOC designs for different base classifiers.

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(b) Classification performance for each group using *FLDA*

(c) Classification performance for each group using Discrete Adaboost

(d) Classification performance for each group using Linear *SVM*
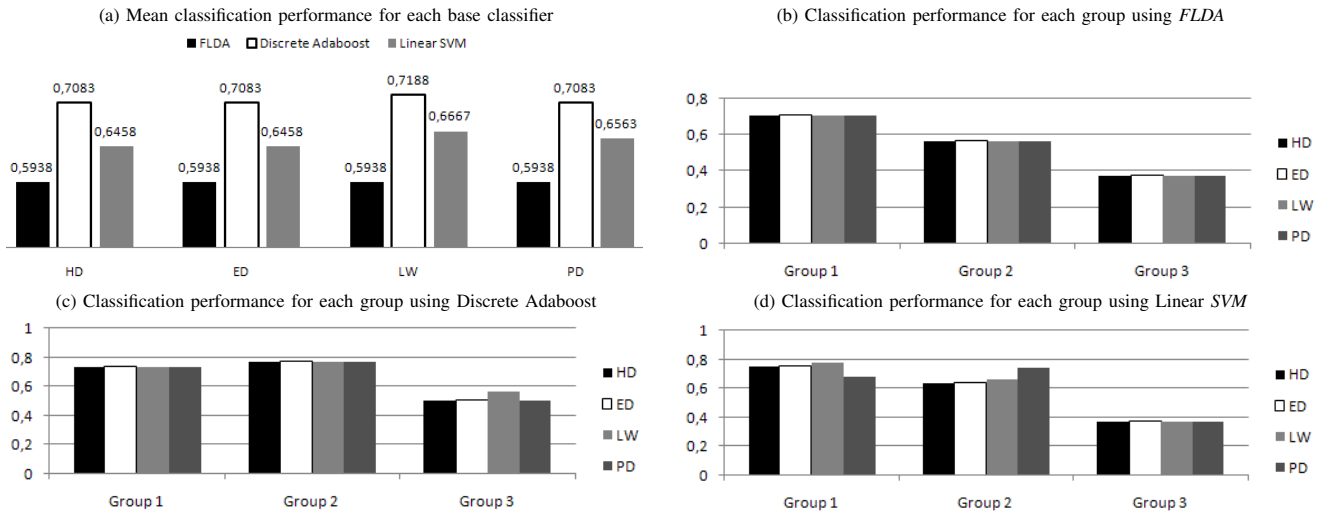
Fig. 5.   Leave-one-patient-out classification using one-versus-one ECOC design (HD: Hamming decoding, ED: Euclidean decoding, LW: Loss-Weighted decoding, PD: Probabilistic decoding) for the three groups with Chagas' disease.

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