Fractionated Electrograms and Rotors Detection in Chronic Atrial Fibrillation Using Model-Based Clustering

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Abstract— **The identification of atrial fibrillation (AF) substrates is needed to improve ablation therapy guided by electrograms, although mechanisms that sustain AF are not fully understood. Detection of complex fractionated atrial electrograms (CFAE) is used for this purpose. Nonetheless, efficacy of this method is inadequate in the case of chronic AF. Recent hypothesis proposes the rotors as fibrillatory substrate. Novel approaches seek to relate CFAE with rotor; nevertheless, such methods are not able to identify the associated substrate. Furthermore, the patterns that characterize CFAE generated by rotors remain unknown. Thus, tracking of rotors is an unsolved issue. In this paper, we propose a non-supervised method to find patterns associated with fibrillatory substrates in chronic AF. We extracted two features based on local activation wave detection and one feature based on non-linear dynamics. Gaussian mixture model-based clustering was used to discriminate CFAE patterns. Resulting clusters are visualized in an electroanatomic map. We assessed the proposed method in a real database labeled according to the level of fractionation and in a simulated episode of chronic AF in which a rotor was detected. Our results indicate that the method proposed can separate different levels of fractionation in CFAE, and provide evidence that clustering can be used to locate the vortex of the rotors. Provided approach can support ablation therapy procedures by means of CFAE patterns discrimination.**

I. INTRODUCTION

Atrial fibrillation (AF) that is the most common sustained arrhythmia and encountered affects 2% of the population, and its incidence is increasing. AF is associated with thromboembolics events and increased rates of death. Rotor hypothesis is one of the most recent approaches to explain the mechanisms that maintain the permanent and persistent AF. Accordingly, AF is a consequence of the continued activity of rotors turning at high frequency around an unexcitable core [1]. Ablation has revolutionized the treatment of AF, this procedure is performed using catheters and is guided by electro-anatomical maps. Ablation treatment aims to avoid the formation and maintenance of fibrillatory conduction, by generating lesions sets on the heart tissue which cause blockage of electrical impulse propagation. However, in the case of chronic AF, this therapy is not entirely successful, because the etiological mechanisms that sustain the arrhythmia are not entirely clear [2].

Detection of complex fractionated atrial electrograms (CFAE) has been proposed as a tool to locate arrhythmogenic substrates. Therefore, corresponding anatomical sites are used as targets for ablation [3]. Methods to detect CFAE have been developed, mainly including firsly characteristics based on time intervals and amplitude [3], and latterly, entropy measures including the Shannon entropy [4] and approximate entropy [5]. Nonetheless, there is not enough evidence to ensure that CFAE are related with rotors in chronic AF, since different levels of fractionation are not well defined by physicians [2]. Specific signal patterns that identify rotors and other arrhythmogenic substrates remain unidentified, thus, the detection of rotors is still an open issue.

In this paper, we propose a method based on clustering using Gaussian mixture models (GMM) to discriminate different levels of fractionation. The method is used to identify different unknown patterns in CFAE in order to generate electro-anatomic maps that allow locating the rotor vortex.

II. METHODS

A. Clustering with Gaussian Mixture Model

GMM assumes that the multidimensional probability distribution function (PDF) is the sum of Gaussians. Usually, Expectation-Maximization (EM) is used to learn the parameters of the model that maximize the likelihood of the data. Also, Bayesian Information Criterion (BIC) is used to select the number of Gaussians. However, if the number of mixture components is overestimated, it can be combined hierarchically according to an entropy criterion [6].

B. EGM Signal Feature extraction

Analysis of fractionation is used to describe CFAE. Physicians usually represent the fractionation levels using descriptive characteristics such as peak count and time intervals. The algorithm described by Kremen et al [7] to detect and evaluate local activation waves (LAW) was implemented in order to obtain some descriptive characteristics. Discrete Wavelet Transform (DWT) was used to search for segments with near-field and far-field activity. Afterward, two features were calculated, the activation segment width (AW-width) and the

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number of zero crossing points in the activation segments (ZC-AW). Approximate Entropy (ApEn) was calculated as a third feature in order to capture information about the non-linear dynamic behaviour of CFAE. ApEn is a non-linear statistic proposed by Pincus [8] that quantifies the complexity of signals. Therefore, a set of three features were computed.

III. Experimental set-up

In this paper, two sets of intracardiac electrogram (EGM) signals were used to verify the performance of the proposed methodology. Firstly, a database composed by EGM from patients indicated for radiofrequency ablation of AF. AF signals in this database were divided by physicians into 4 classes according to the level of signal fractionation. Secondly, electrograms acquired from a simulated chronic AF episode. In both experiments, 3 features of EGM signals were extracted. Clustering using GMM was performed in order to discriminate different levels of fractionation. BIC was used to select the number of components. In the second experiment, using the information of the model, a pattern dependent electro-anatomic map was constructed, where each color of the map represented a group found by clustering and suggested a different CFAE pattern. With the purpose of locating rotors in this map, the color assigned for each cluster was located at a position where the corresponding signal was measured. Finally, the rotor was associated with one cluster.

A. Experimental data-set

A database constructed by "Staedtisches Klinikum Karlsruhe" from Germany was used in this project [9]. The database holds 429 records acquired during pulmonary vein isolation using a multipolar circular catheter. These signals were recorded at 1.2 kHz sampling rate. All patients were indicated for radiofrequency ablation of AF. The data were filtered at 30-250 Hz, and the remaining baseline wander and high noise was reduced by the wavelet decomposition method described in [9]. The database was independently labeled by two different electrophysiologists (EPs). Non-fractionated EGM signals were considered as level 0 (C0). The fractionated signals were categorized into three levels of fractionation: mild, intermediate and high. C1, C2 and C3 respectively, see Fig. 2. The 429 signals were distributed into the classes of fractionation as follows: 153 signal in C0, 75 signals in C1, 148 signals in C2 and 53 signals in C3.

B. Simulated episode of AF and electrograms

A realistic 3D model of the human atrium was developed in an earlier work [10], and included the main anatomical structures, fiber orientation, electrophysiological and conduction heterogeneity and anisotropy. The Courtemanche-Ramirez-Nattel-Kneller membrane formalism was implemented to reproduce the cellular electrical activity. Changes in the maximum conductance of different ionic channels of human atrial cells observed in experimental studies of chronic AF were incorporated into the action potential model to reproduce the atrial electrical remodeling.

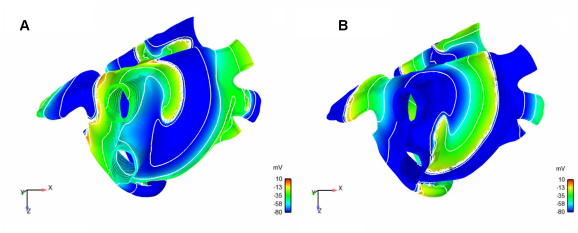


Fig. 1. Propagation of action potential in simulated episode of AF. A and B are frames captured in different times

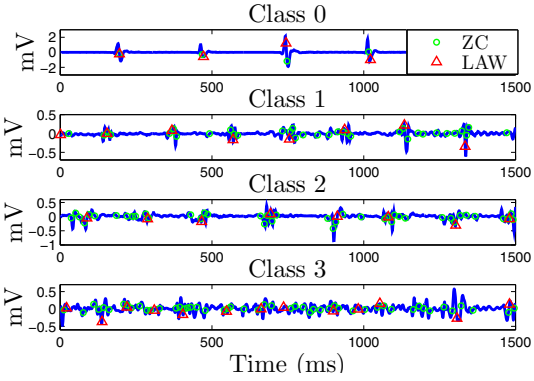


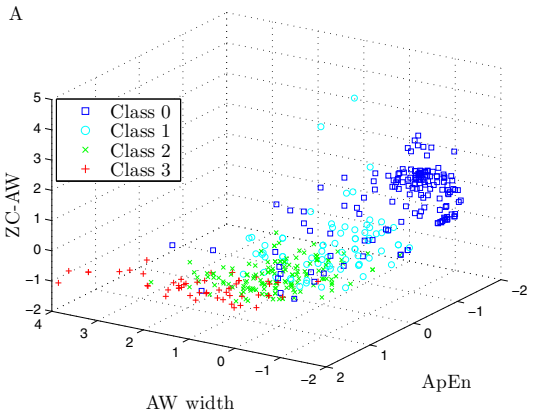
Fig. 2. Samples of the considered EGM recording classes. LAW points and Zero Crossing Points (ZC) detected by the descriptive feature extraction algorithm are shown.

A chronic AF episode was simulated, and unipolar EGMs in different points of the atrial surface were recorded at 1 kHz for the last 4 seconds of AF simulation, as described by Tobon et al [10]. A set of 620 Bipolar signals were generated by the subtraction of two adjacent unipolar EGM separated by 1 mm. Fig. 1 shows 2 simulation frames in which the action potential propagation is represented by colors and one rotor could be seen in the posterior wall of the left atrium.

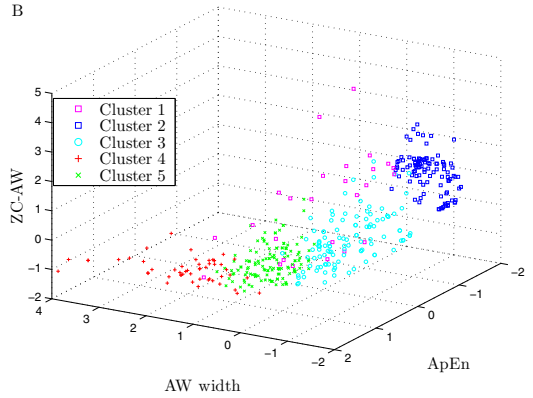
C. Features extraction

To compute the descriptive features based in LAW detection explained above, we used Discrete Wavelet Transform with 3 decomposition levels and using a Coiflet 4 as mother wavelet. The signal coefficients of detail were reconstructed at level 3 (L3). L3 was normalized to its maximum absolute value and thresholded at $th = \varphi$. Parameter φ was adjusted using an adaptive threshold, as given in [11]. Adjacent activation with intersegment space $< 40ms$ was joined as a LAW segment. The maxima and minima points were located using the zero crossing detection in the first derivative. Only max-min pairs with amplitude higher than a threshold ϵ and corresponding ZC points were counted, see Fig. 2. Parameter ϵ was selected according to the process described in [12].

Approximate entropy (ApEn) was calculated using the following parameters $m = 3, r = 0.38$ as was evaluated in a previous work. A feature matrix $\mathbf{\Theta} \in \mathbb{R}^{429\times 3}$ was obtained by arranging the features of all the observations in the database or the simulated event. $\mathbf{\Theta_1}$ corresponds to signals from database and $\mathbf{\Theta_2}$ to signals from the simulated



(a) Annotated labels



(b) Cluster labels

Fig. 3. Feature space in $\mathbb{R}^3$ of $\mathbf{\Theta_1}$ - a. Distribution of the classes using labels annotated by physicians. Note that classes are overlapped. b. Clusters found using 5 Gaussians.

episode of AF.

D. Clustering

Normal mixture modeling via EM was implemented using mclust package [13] in R. A parameterized covariance structures VVI (volume: variable, shape: variable and orientation: diagonal) was evaluated and BIC was used to select the number of Gaussians. According to BIC criterion, the parameter K, number of Gaussians, was established in $K = 5$. Using the same criterion, $K = 9$ was selected to the set of features $\mathbf{\Theta_2}$.

IV. Results and Discussion

A. Clustering of EGM from database

Fig. 3(a) shows the distribution of $\mathbf{\Theta_1}$ in a $\mathbb{R}^3$ cartesian coordinate system according to labels assigned by physicians. The boundaries between classes are soft because the patterns that correspond to each class are not clearly defined in medical practice. Fig. 3(b) shows the distribution of $\mathbf{\Theta_1}$ using the groups found by clustering using GMM.

BIC process identified 5 clusters. We suggest that levels of fractionation could be explained better using more than 4 scales to include different patterns. Table I shows a confusion matrix with the results of the fractionation levels discrimination. Table II shows obtained results for evaluating sensitivity and specificity of the clustering, where each cluster was labeled with the class corresponding to the largest number of detected records. The correct rate was 71.10%. This result confirms the application of clustering with GMM for discriminating EGMs between different levels of fractionation.

TABLE I
Confusion matrix of GMM clustering

	Class 0	Class 1	Class 2	Class 3
Cluster 1	19	7	0	0
Cluster 2	108	0	0	0
Cluster 3	22	50	39	1
Cluster 4	1	0	16	35
Cluster 5	3	18	93	17

TABLE II
Performance of clustering with GMM

	Sensitivity (%)	Specificity (%)
Class 0	83.01	97.46
Class 1	66.67	82.49
Class 2	62.84	86.48
Class 3	66.04	95.48

B. Rotor detection based on clustering

Clustering with GMM was performed for the set $\mathbf{\Theta_2}$ from the simulated EGM signals. Fig. 4 shows a color map in which the red area corresponds to a cluster composed by signals with a higher level of fractionation. This area corresponds to one rotor vortex which can be seen in the frame of action potential propagation extracted from the 3D model (R area in Fig. 4). The electro-anatomic color map was built using one color for each group found by clustering with GMM. The map is represented on the plane using the coordinates axis x and z from the posterior wall of the left atrium where the signal was recorded in the simulated model.

Fig. 5 shows the distribution of $\mathbf{\Theta_2}$ according to clusters optimized by EM with $K = 9$ components. In this case, overestimation of the number of components was evaluated using entropy criterion [6]. As a result, clusters 3, 4, 6, 8 and 9 can be joined in the same cluster, and then, this group is modeled by a Gaussian mixture of 5 components and corresponds to signals with regular activation (non-CFAE) present in sites outside the rotor area. These results suggest that clustering could be used to locate arrhythmogenic substrates in AF, such as rotors.

Supervised learning methods have been proposed to detect CFAE [14], [15] and to classify levels of fractionation. Nevertheless, because fractionation definition is unclear [2], [3], the labeled signals used in the training process, usually depend on subjective perception of EGM fractionation by the physicians. This issue become a restriction for the clinical usage of supervised approach. On the other hand, our results

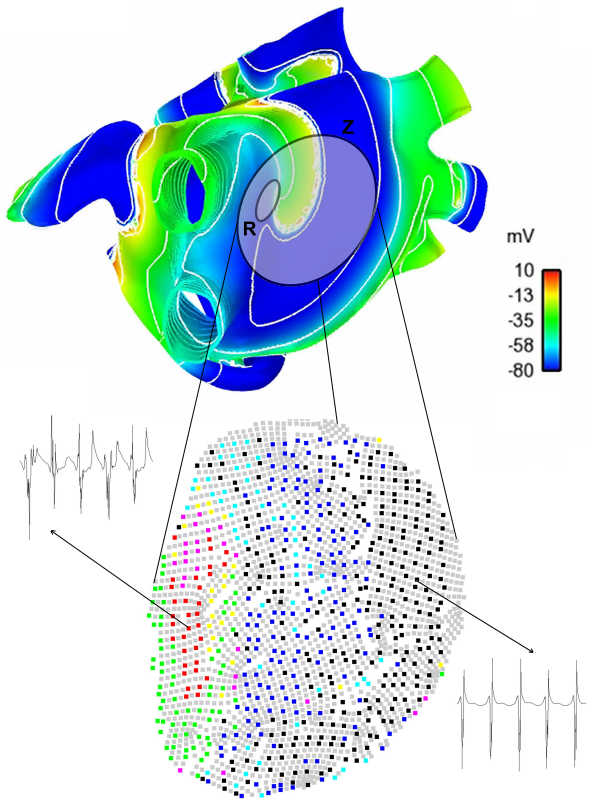


Fig. 4. Top: Action potential propagation in the model where a rotor is located in the region marked by ellipse R. Bottom: Color map generated by clustering applied to bipolar signals from region Z. Cluster labels are represent by colors. The red cluster corresponds to rotor tip localization (R). Samples of two signals are shown, a fractionated signal from the rotor tip and a regular activation pattern from non-rotor area. Note that different clusters are located around the rotor vortex, organized according to the degree of fractionation.

indicate that a non-supervised method, such as GMM-based clustering, can be used to detect patterns in CFAE related with rotors without using a priori information of the data.

V. CONCLUSIONS

Our analysis evidences that GMM-based clustering applied to relevant EGM features is able to fulfill the following conditions: i) discriminate CFAE with different levels of fractionation, and ii) locate rotors in a simulated episode of chronic AF. These findings indicate that the method proposed can be the basis of a new tool to detect arrhythmogenic substrates in AF.

Future studies should evaluate the used of soft clustering and the implementation of a feature selection scheme to include other features. The method requires further evaluations using several simulations, including meandering rotors and other sites around the atria to evaluate repetitiveness and sensibility. Additionally, clinical evaluation is needed to find real patterns presents in arrhythmogenic subtracts and to provided evidence of the effectiveness to locate target sites for ablation.

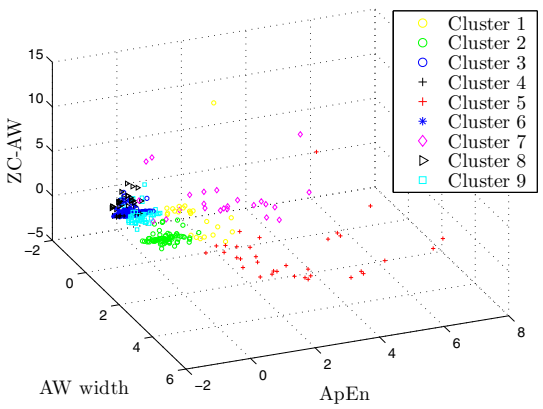


Fig. 5. Feature space in $\mathbb{R}^3$ of $\mathbf{\Theta_2}$. Colors represent groups found by clustering with 9 components. Note that distribution of clusters 5 and 7 tends to locate away of other densities, these clusters are correspond to EGM a with high level of fractionation.

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