Classification of atrial electrograms in atrial fibrillation using Information Theory-based measures

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Introduction

Classification of complex fractionated atrial electrograms (CFAE) is crucial for the study of atrial fibrillation and for the development of treatment strategies, because these electrophysiological phenomena represent a common target for radiofrequency ablation. Since the description of CFAEs in 2004, the scientific community have been focused their efforts into its characterization and automatic classification considering the degree of fractionation, a clinical scale used in ablation procedures. Endocardial sites associated to CFAEs are usual targets in ablation therapy, as is though that they play a role in maintenance of the arrhythmia. **Objective:** The objective of this work is the characterization of short term atrial electrograms using nonlinear dynamics measures, helping in the automatic classification of electrograms.

Epidemiology

Atrial fibrillation (AF) is the most common cardiac arrhythmia after miocardial infarction. It is characterized by a rapid and irregular activation of the atrium, at rates between 5 and 10 Hz. The principal mechanisms of initiation and maintenance of AF are reentrant activity and focal ectopic firing. AF induces changes in the cardiac tissue, favoring the evolution to persistent forms with complex reentrant mechanisms, which are irreversible and more resistant to therapy [1]. In most cases, AF have associated a cardiac disease (heart failure, hypertensive heart disease, valvular disease, ischemic heart disease, among others) and can be predisposed by several extracardiac conditions, as alcohol consumption, hyperthyroidism, obesity, genetic and hereditary factors. The development of persistent forms of AF, together with the associated comorbidities, results in a complex clinical condition.

Atrial electrograms

Intracavitary electrograms from left atria are mapped to characterize the electrical activity of different sectors of the atrial wall. Traditionally, mapping of AF has used electrodes that can provide high resolution at multiple sites. The dataset used in this work consists of **113 atrial electrograms recordings** of 1.5 seconds of duration from left-atrial endocardial mapping in 12 patients with persistent AF. These signals were classified by three expert electrophysiologists into four classes according to signal regularity, from C0 (non fractionated) to C3 (high degree of fractionation).The general classification of the dataset was constructed as the majority vote of the three experts in each signal. The complete dataset will be referred as **Full dataset**, whereas the subgroup containing only the electrograms that were classified identically by the three experts (68 of the 113 signals) will be referred as **Reduced dataset**. Three sets of pre-processed signals are available in the dataset: raw signals, denoised signals and a set of filtered signals in which CFAEs events were emphasized [2, 3].

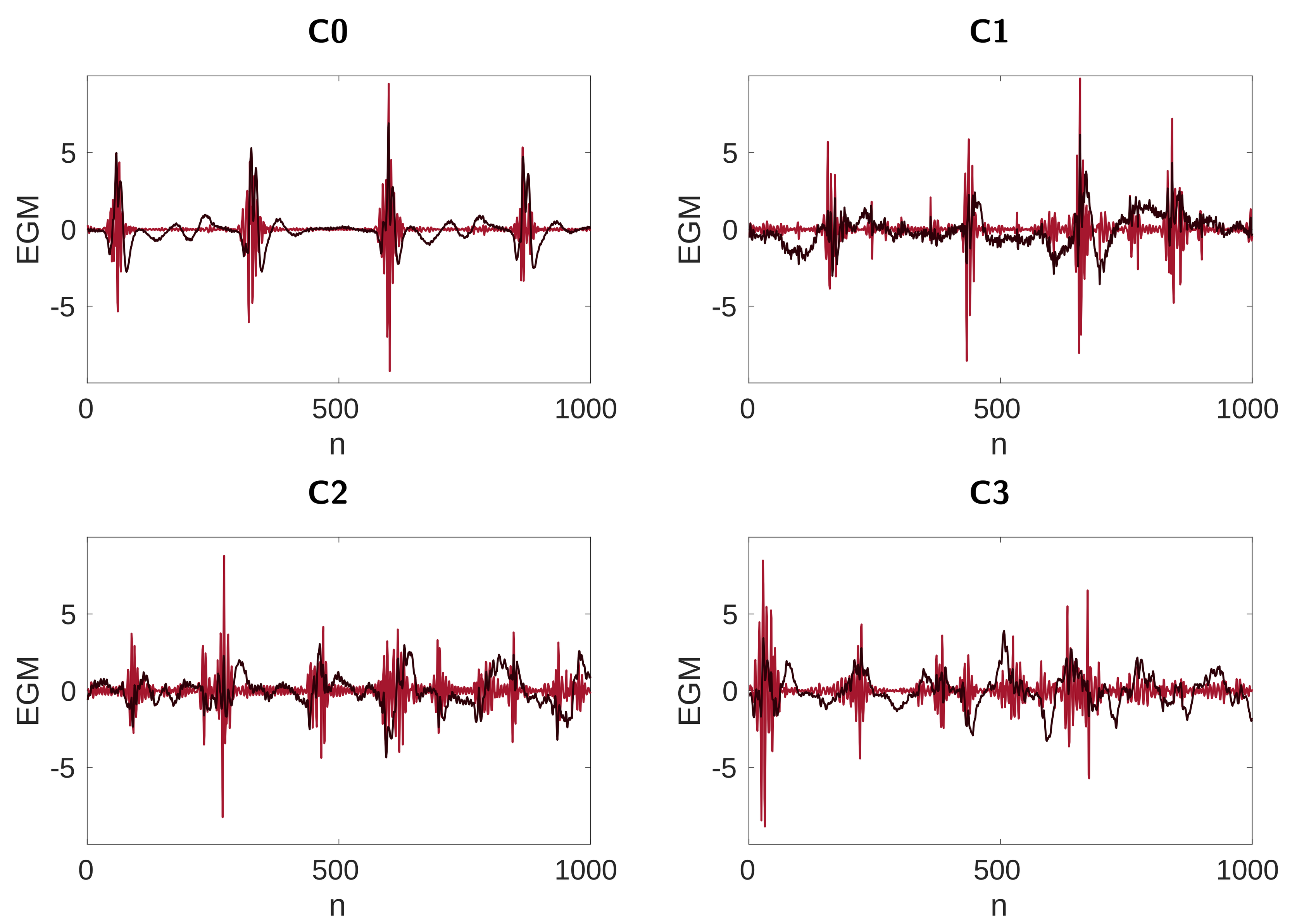

Figure: Representative EGMs of each class of fractionation, original and filtered signals, emphasizing CFAEs events.

Complexity and Information measures

Signals were normalized to zero mean and unitary variance ($\mu = 0, \sigma = 1$). The embedding lag ($\tau = 4$) was determined using the mutual information function, and was used to construct state vectors for the features that need it. The following measures were calculated: Approximate entropy, Dispersion entropy, Fuzzy entropy, Permutation entropy, Tsallis entropy, Shannon entropy, Renyi entropy and Lempel-Ziv complexity. A total of **245 features** was calculated to each signal, considering the parameters variation in each measure.

Feature selection

The algorithm called Neighborhood Component Analysis (NCA) was used for selecting features maximizing prediction accuracy. In this work we selected the gradient ascent technique to maximize the classification accuracy with a regularization term [4]. We estimate the feature weights in a 10-fold scheme searching the best value of the regularization parameter minimizing the mean square error in classification. We applied a relative threshold to select the features with maximum weights correspondent to each classification task.

Results

A 10-fold cross validation scheme was applied to test the classification using 4 different classifiers: linear and quadratic discriminant, and linear and quadratic SVM. Every performance measure is expressed with its mean value μ and standard deviation σ, obtained from 50 realizations of each classifier.

	Classification performance over 4 classes Linear SVM - Reduced dataset			
	Accuracy (μ and σ)	Sensitivity (μ and σ)	Specificity (μ and σ)	AUC ROC
C0	98.15% (0.59%)	99.89% (0.06%)	97.41% (0.79%)	0.99
C1	93.06% (1.27%)	84.08% (2.80%)	96.54% (1.19%)	0.98
C2	91.89% (1.13%)	84.07% (2.19%)	96.00% (1.05%)	0.96
C3	96.85% (0.04%)	99.95% (0.05%)	96.32% (0.05%)	0.99

Table: Results on classification over 4 classes of fractionation in reduced dataset.

In the discrimination of C3 from the rest of the classes of electrograms, the accuracy was over 95% for both full dataset and reduced dataset.

Classification performance (C0+C1+C2 vs C3)						
	Full dataset			Reduced dataset		
Classifiers	Acc	Se	Sp	Acc	Se	Sp
Linear Discriminant	95.29% (0.77%)	97.02% (0.65%)	81.28% (3.79%)	93.56% (0.72%)	79.23% (3.34%)	96.47% (0.3%)
Quadratic Discriminant	96.32% (0.95%)	96.64% (0.55%)	93.83% (7.74%)	94.68% (1.02%)	97.44% (4.89%)	94.36% (0.9%)
Linear SVM	94.40% (0.88%)	97.04% (0.57%)	82.06% (4.83%)	97.06% (0.01%)	99.98% (0.0015%)	96.61% (0.002%)
Quadratic SVM	96.18% (0.94%)	97.03% (0.37%)	88.80% (6.33%)	96.15% (0.83%)	94.36% (5.06%)	96.48% (0.39%)

Table: Results on classification of C3 signals over the rest of classes of fractionation.

Features selected using NCA to classify electrograms into 4 classes were:

- Lempel-Ziv complexity, quartile-value threshold - Denoised signals
- Fuzzy entropy, $m = 2$ - Raw Signals
- Dispersion entropy, $m = 2, c = 4$ - Filtered signals

In discrimination of C3 signals in the full dataset, the selected features were:

- $ApEn_{max}$ - Approximate entropy with Heaviside kernel - Raw signals
- h_{max} - Approximate entropy with Heaviside kernel - Filtered signals
- h_{max} - Modified approximate entropy with Heaviside kernel - Filtered signals,

whereas in the reduced dataset the used features were:

- h_{max} - Approximate entropy with Gaussian kernel - Raw signals
- h_{max} - Approximate entropy with Heaviside kernel - Denoised signals
- $ApEn_{max}$ - Approximate entropy with Gaussian kernel - Denoised signals

Discussion and Conclusion

Considering classification into 4 classes, in the work of Kremen et al. [5] only the classification error is reported, both in each class (classes C0 and C1 discriminated with 0% error, C2 with 14.3% and C3 with 9.1%) and average over all classes (~5.9%), however it is not specified if shown errors were obtained in full or reduced dataset. Results presented in [2] about discrimination of signals in class C3 from the rest reported sensitivity of 81.8% and specificity of 90.2%, while results of this work shows sensitivity of 96.64%, specificity of 93.83% and accuracy of 96.32%. Our results over these different classification experiments show the usefulness of combining several information theory based measures in atrial fibrillation electrograms analysis. We consider that the clinical use of an adapted version of this framework can help in the determination of sites associated to the generation and maintenance of atrial fibrillation.

References

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