

# Comparative Study of Non-Invasive Organization Estimation Strategies to Predict Spontaneous Termination of Atrial Fibrillation

R Alcaraz<sup>1</sup>, JJ Rieta<sup>2</sup>, A Martínez<sup>1</sup>

<sup>1</sup>Innovation in Bioengineering Research Group. University of Castilla-La Mancha, Cuenca, Spain

<sup>2</sup>Biomedical Synergy, Electronic Engineering Dept., Universidad Politécnica de Valencia, Spain

## Abstract

*In the present work, three methods based on the Sample Entropy (SampEn) non-invasive organization estimation of atrial fibrillation (AF) to predict its spontaneous termination are compared making use of the same patient's database. In the first strategy, the atrial activity (AA) is obtained through QRST cancellation. Next, the main atrial wave (MAW) of the AA is obtained by selective filtering centered on the dominant atrial frequency (DAF), thus yielding the time series for SampEn computation. In the second strategy, an equivalent wave to the MAW is obtained by applying seven levels of discrete wavelet decomposition to the AA. The sub-band containing the DAF is reconstructed back to time domain and evaluated with SampEn. In the last strategy, the time series is obtained as the concatenation of TQ segments, free of QRST complexes. The three methods were validated with a database containing a training set of 20 AF recordings, with known termination properties, and a test set of 30 recordings. For the learning set, sensitivity values were 100%, 80%, and 80% and specificity values were 90%, 90%, 100% for the methods based on selective filtering, wavelet transform and concatenation of TQ segments, respectively. Regarding the test signals, a sensitivity of 93.75% and a specificity of 85.71% were provided for the three methods. These coherent outcomes allowed us to conclude that the three techniques can estimate robustly AF organization and predict successfully paroxysmal AF termination.*

## 1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting 1% of the general population [1]. Considering its prevalence with age [2], this arrhythmia affects up to 15% of the population older than 80 and has an incidence that doubles with each advancing decade after 40/50 years. Paroxysmal (spontaneously terminated) AF (PAF) is, by evidence, antecedent to persistent AF, which requires a pharmacological or external electrical intervention (car-

dioversion) to allow its termination [3]. Persistent AF patients present a high risk of embolic accidents [4] and about 18% of paroxysmal AF degenerate into persistent AF in less than 4 years [5]. Therefore, the early prediction of AF maintenance is crucial, because appropriate interventions may terminate the arrhythmia and prevent AF chronification. In contrast, the prediction of spontaneous AF termination could avoid unnecessary therapy, reduce the associated clinical costs and improve the patient's quality of life.

To date, several methods to predict spontaneous PAF termination from surface ECG recordings have been proposed. Three of them are based on the Sample Entropy (SampEn) non-invasive organization estimation of AF [6–8]. However, each one of them uses different signal transformations to generate the final time series over which SampEn is applied. The present work compares these strategies making use of the same patient's database.

## 2. Materials

The used database contained 50 one minute and two leads (II and V1) electrocardiogram (ECG) recordings, which were available in Physionet [9]. They were extracted from 24-hour Holter recordings from 50 different patients. The database included non-terminating AF episodes (group N), which were observed to continue in AF for at least one hour following the end of the excerpt, and AF episodes terminating immediately after the end of the extracted segment (group T). Recordings were divided into a learning and a test set. Next, 10 labelled recordings of each group formed the learning set. For each analyzed strategy, an optimal threshold, which should allow to discern between terminating and non-terminating PAF episodes, was defined making use of the learning set. Finally, the test set was composed with the remaining 30 recordings.

These ECG recordings were preprocessed to improve later analysis. Firstly, baseline wander was removed making use of bidirectional high pass filtering with 0.5 Hz cut-off frequency [10]. Secondly, high frequency noise was reduced with a eight-order bidirectional IIR Chebyshev low

pass filtering, whose cut-off frequency was 70 Hz. Finally, powerline interference was removed through adaptive filtering, which preserves the ECG spectral information [11].

### 3. Methods

#### 3.1. Selective Filtering Organization (SFO)

The main goal of this strategy was to obtain the main atrial wave (MAW) of the AA [6]. This wave can be considered as the fundamental waveform associated to the AA, its wavelength being the inverse of the AA main frequency [12]. For this purpose, AA was firstly extracted from surface ECG recordings making use of the averaged QRST template cancellation method [13], see Fig. 1. Next, the residual signal power spectral density (PSD) was calculated using Welch Periodogram. A Hamming window of 4096 points in length, a 50% overlapping between adjacent windowed sections and a 8192-points Fast Fourier Transform (FFT) were used as computational parameters as suggested by previous works [14]. The largest amplitude frequency within the 3–9 Hz range was selected as the dominant atrial frequency [12] and the MAW was obtained by applying a selective filtering to the AA signal centered around this frequency [6]. Through these steps, the noise present in the AA was considerably reduced and the AA main features were selected. Finally, SampEn of the MAW was computed and compared with a threshold to discriminate between terminating and non-terminating PAF episodes.

To prevent distortion, a linear phase FIR filter was used [15]. Chebyshev approximation was preferred because all the filter parameters can be suitably fitted and minimum ripple in the pass and stop bands was needed. Several experiments showed that the best results were obtained with a 3 Hz bandwidth and 768 filter coefficients [6].

#### 3.2. Wavelet Organization (WTO)

Wavelet analysis transforms the signal under investigation into another one including both frequency and time domain information. Hence, the Wavelet Transform (WT) allows to isolate certain time-frequency characteristics of a signal in limited decomposition coefficients [16]. This fact permits to observe regularity variations in the AA signal, that would be left masked in other cases [17]. Thereby, a new methodology based on WT to reduce noise and able to select the main features of the AA signal obtained from surface ECG recordings has been also proposed [8]. In this case, the AA was also obtained making use of the averaged QRST template cancellation method [13], see Fig. 1. Next, this signal was decomposed using discrete WT in different detail and approximation coefficients, and only the frequency band containing the dominant atrial fre-

quency, which was obtained from the AA PSD calculated using Welch Periodogram as for SFO, was reconstructed back to the time domain. Finally, SampEn of this signal was calculated and compared with a SampEn threshold, showing relevant differences between terminating and non-terminating AF episodes.

Regarding wavelet decomposition parameters, seven levels were applied, since approximation and low frequency detail scales can cover the typical AA frequency range, which is around 3–9 Hz [18]. In addition, a fourth-order biorthogonal wavelet family was used, because it provided the best classification results [8].

#### 3.3. TQ Intervals Organization (TQO)

Organization analysis of TQ segments, free of QRST complexes, has been also performed with SampEn to predict PAF behavior [7], thus, reducing the ventricular residual effect on the prediction. In this method, all R waves were firstly detected making use of the Pan-Tompkins technique [19], see Fig. 1. Next, the Q waves onset was determined through an algorithm that exploits the relatively quiescent interval immediately before ventricular depolarization [20]. Within a 120 ms interval before the R peak, the point at which the amplitude range, within a 30 ms sliding window, fell to its minimum was selected as Q onset [21]. The computation of an indicator related to the area covered by the T wave was used to determine T waves ending. The maximum of the computed indicator inside each cardiac cycle was the T wave ending. The algorithm mainly consisted of an integration operator over a sliding window and was implemented as a simple finite impulse response (FIR) filter [22]. For each heartbeat, the segment between T wave ending and Q wave onset was extracted and its average value was removed. The elimination of sudden transitions between TQ segments is crucial. These transitions occur after the heartbeat and provoke artificial frequency components near to the original ventricular rate, thus degrading AA organization estimation. To avoid sudden transitions when the TQ segments were consecutively joined, these segments were multiplied by a softened extremes window, whose amplitude increases linearly from 0 to 1 during the first 10% of its length, is maintained to 1 during the next 80%, and finally decreases linearly from 1 to 0 during the last 10%. Finally, a 10% overlapping allowed us to obtain soft unions between consecutively joined segments. Thus, a continuous signal, which offers the main AA characteristics such as amplitude, regularity and time waveform, was obtained [7]. Finally, the signal organization was estimated making use of SampEn and compared with a SampEn threshold to discern between terminating and non-terminating PAF episodes.

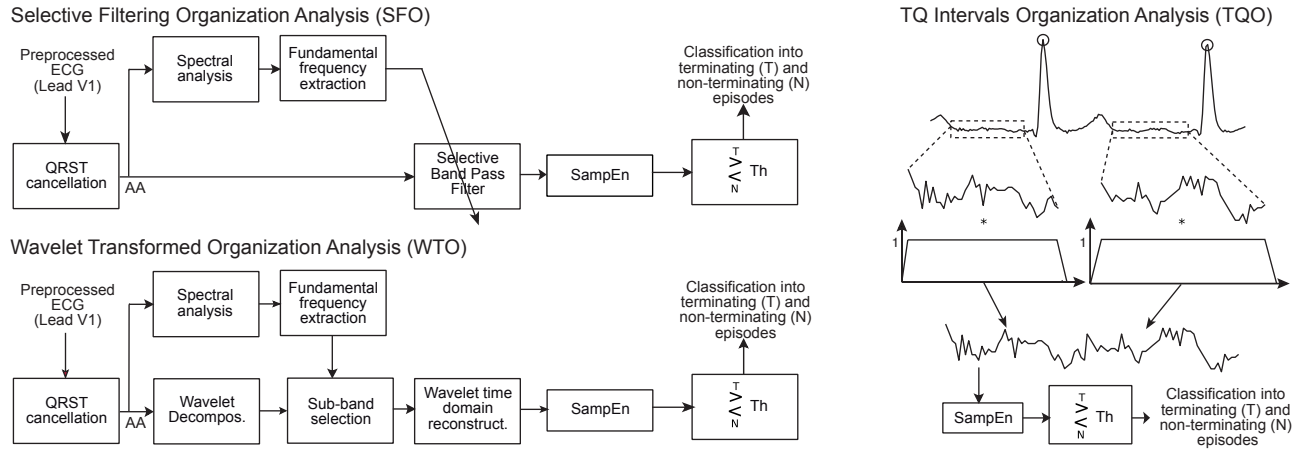


Figure 1. Block diagrams describing how the three methods compared in the study operate to classify between terminating and non-terminating atrial fibrillation episodes.

## 4. Results

The optimum SampEn threshold for each analyzed methodology was selected from the training set to improve the sensitivity/specificity pair according to the ROC plots [23]. Different thresholds or cutoff points (SampEn values) were selected and the sensitivity/specificity pair for each one of them were calculated. Sensitivity (the true positive rate) is the non-terminating episodes proportion correctly classified (SampEn value higher than the cutoff point), whereas specificity (the true negative rate) represents the terminating AF episodes percentage correctly recognized (SampEn value lower than the cutoff point). The closest point to 100% sensitivity and specificity was selected as optimum SampEn threshold.

The three methodologies were applied to the learning signals obtaining 100% sensitivity and 90% specificity for SFO, 80% sensitivity and 90% specificity for WTO and 80% sensitivity and 100% specificity for TQO, respectively. For the three strategies, ROC curves obtained with the learning set provided 0.085, 0.089 and 0.265, respectively, as optimum SampEn discrimination thresholds between terminating and non-terminating PAF episodes. Note that 95% (19 out of 20), 85% (17 out of 20) and 90% (18 out of 20), respectively, of the learning recordings were correctly discriminated.

Regarding the test set, the same three recordings were incorrectly classified by the three studied strategies, thereby, the obtained results consistency was increased. Consequently, 90% (27 out of 30) of the test signals were correctly classified, obtaining 93.75% sensitivity and 85.71% specificity. Therefore, PAF behavior of 92% (46 out of 50), 88% (44 out of 50) and 90% (45 out of 50) of all analyzed episodes was correctly predicted for SFO, WTO and TQO, respectively.

## 5. Discussion and conclusions

The three analyzed methods focus on reducing the presence of noise, ventricular residua and other nuisance interferences in the AA signal prior to SampEn application as estimator of AF organization. To this respect, in order to avoid the ventricular residua present in the AA signal obtained from surface ECG recordings making use of QRST cancellation methods [24], the organization of AA segments free of QRST complexes with SampEn was proposed and analyzed [7]. However, because of TQO method could obtain negative outcomes when TQ interval are vanished at very high heart rates [7], WTO and SFO strategies were proposed to reduce noise and ventricular residua in the AA signal obtained with ventricular cancellation methods [6, 8].

Nevertheless, the similarity among the results obtained with the three methods increases their consistency, and allows us to conclude that the three techniques can estimate robustly AF organization and predict successfully paroxysmal AF termination. Additionally, the outcomes corroborate that a suitable noise reduction in the AA signal prior to its organization estimation via non-linear regularity indexes is necessary to predict successfully PAF termination.

However, the best predictive ability was obtained through the MAW organization analysis. Thereby, it could be considered that the MAW contains the most important information about spontaneous PAF termination and lower noise than the AA obtained directly from QRST cancellation. Thus, an in-deep MAW analysis should improve understanding of PAF termination mechanisms.

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Address for correspondence:

Raúl Alcaraz Martínez  
E. U. Politécnica de Cuenca  
Campus Universitario  
16071 Cuenca (Spain)  
raul.alcaraz@uclm.es