Predicting Spontaneous Termination of Atrial Fibrillation with Time-Frequency Information

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Abstract

Our approach to predicting spontaneous termination of atrial fibrillation (AF) is based on parameters derived from the time-frequency distribution of the residual ECG signal, resulting from spatiotemporal cancellation of QRST complexes. Each consecutive, logarithmically scaled spectrum of the time-frequency distribution of the residual ECG is modeled as a frequency shifted and amplitude scaled version of a spectral profile. Parameters characterizing AF, such as fundamental frequency, amplitude, and waveform of the fibrillation waves, are then extracted from the spectral profile. The waveform of the spectral profile is used to distinguish AF from sinus rhythm and noise, so that occasional episodes of sinus rhythm and noise can be excluded. Using these parameters, 95% of the ECGs from the training set, and 90% from the test set was correctly classified as non-terminating and terminating AF respectively.

1. Introduction

Atrial fibrillation is the most common arrhythmia encountered in clinical practice, with a prevalence of 0.4% of the general population and over 6% of people over 80 years old [1]. Atrial fibrillation can be subdivided into different forms, namely, (1) paroxysmal AF, i.e. self-terminating AF within 7 days, (2) persistent AF in which interventions are required to terminate fibrillation, and (3) permanent AF in which sinus rhythm cannot be restored or maintained. Studying paroxysmal AF, and identifying onset and termination mechanisms may lead to better pathophysiological understanding of the arrhythmia and, accordingly, more effective therapy. The aim of this work is to investigate the possibility to predict if (or when) an episode of AF terminates spontaneously.

In deriving a set of features which characterize AF, the first step is to extract the atrial activity from the ECG signal. Various methods have been developed, e.g., blind source separation [2], principal component analysis [3], and spatio-temporal cancellation [4] of which the last technique is the most suitable for two-lead Holter-recordings. Spatio-temporal cancellation extends average beat subtraction by aligning the QRST complexes between adjacent leads.

A feature which has been suggested to characterize AF is the fibrillation frequency [3],[5]. Other features are the amplitude and waveform of the fibrillation waves, which may be derived from the spectrum of the atrial activity by analyzing the properties of the fundamental frequency and the harmonics. The exponential decay is a recently presented parameter which quantifies the waveform of the fibrillation waves, using the magnitude of the harmonics [6].

2. Methods

2.1. Log-spectral profile

The logarithmically scaled time-frequency distribution, $\mathbf{q}_l$, of the l:th residual ECG segment [4] is calculated using a non-uniform, short-time Fourier transform [6]. Each spectrum $\mathbf{q}_l$ can be modeled as a frequency shifted, θ_l, and amplitude scaled, a_l, version of a known real-valued spectral profile, $\boldsymbol{\phi}_l$,

$$\tilde{\mathbf{q}}_l = a_l \, \mathbf{J}_{\theta_l} \, \boldsymbol{\phi}_l, \tag{1}$$

where the matrix $\mathbf{J}_{\theta_l}$ performs the frequency shift. The amplitude-scaling parameter a_l and the frequency shifting parameter θ_l can be estimated by minimizing the cost function, $J(\theta_l, a_l)$,

$$J(\theta_l, a_l) = (\mathbf{q}_l - a_l \mathbf{J}_{\theta_l} \boldsymbol{\phi}_l)^T \, \mathbf{D} \, (\mathbf{q}_l - a_l \mathbf{J}_{\theta_l} \boldsymbol{\phi}_l), \tag{2}$$

so that the model, $\tilde{\mathbf{q}}_l$, resembles the true spectrum, $\mathbf{q}_l$, as much as possible. The diagonal $K \times K$ matrix $\mathbf{D}$ is designed to weight the error of the frequency components of $\tilde{\mathbf{q}}_l$ differently, in order to compensate for the logarithmic frequency scaling. Minimization of (2) results in the frequency shifting estimate [6]

$$\hat{\theta}_l = \arg\max_{\theta_l} [\mathbf{q}_l^T \mathbf{D}^{\frac{1}{2}} \mathbf{J}_{\theta_l} \mathbf{D}^{\frac{1}{2}} \boldsymbol{\phi}_l] \tag{3}$$

and amplitude scaling estimate

$$\hat{a}_l = \mathbf{q}_l^T \mathbf{D}^{\frac{1}{2}} \mathbf{J}_{\hat{\theta}_l} \mathbf{D}^{\frac{1}{2}} \boldsymbol{\phi}_l \tag{4}$$

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Computers in Cardiology 2004;31:657−660.

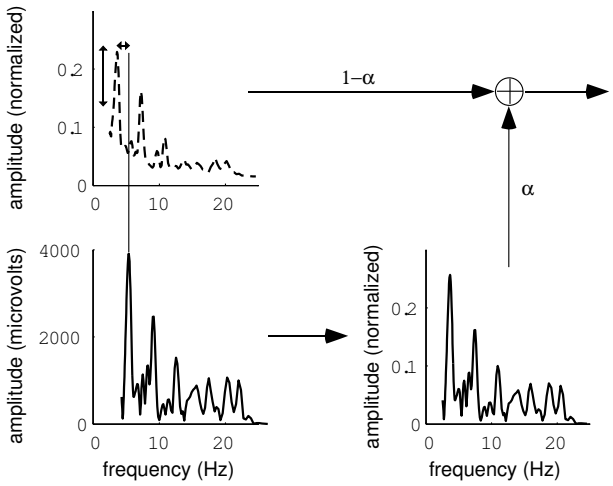

Figure 1. The spectral profile ϕ_l (top) is frequency shifted and amplitude scaled, as marked by the small arrows, to best fit $\mathbf{q_l}$ (bottom left). The spectral profile is then updated by the frequency shifted and amplitude scaled version of $\mathbf{q_l}$ (bottom right).

With the estimated values $\hat{a}_l$ and $\hat{\theta}_l$, we obtain

$$\hat{\mathbf{q}}_l = \hat{a}_l \, \mathbf{J}_{\hat{\theta}_l} \, \boldsymbol{\phi}_l. \tag{5}$$

The initial spectral profile, $\boldsymbol{\phi}_0$ is set to

$$\boldsymbol{\phi}_0 = [\ 0.01 \quad \ldots \quad 0.01 \quad 1 \quad 0.01 \quad \ldots \quad 0.01\ ]^T \tag{6}$$

where $\boldsymbol{\phi}_0$ is 1 at the peak position and 0.01 at all other positions. The spectral profile, $\boldsymbol{\phi}$, is updated through exponential averaging, so that

$$\hat{\boldsymbol{\phi}}_{l+1} = (1-\alpha_l)\hat{\boldsymbol{\phi}}_l + \alpha_l \frac{\mathbf{J}_{\hat{\theta}_l}\hat{\mathbf{q}}_l}{\|\mathbf{J}_{\hat{\theta}_l}\hat{\mathbf{q}}_l\|}, \; l > 0 \tag{7}$$

where the gain α_l set to a positive constant when the signal is reliable, and zero otherwise. Figure 1 illustrates the matching and updating of the spectral profile.

2.2. Time-frequency measures

The *fibrillation frequency*, f_l, is the dominant peak of the residual ECG spectrum, $\mathbf{q}_l$, of segment l. In this case it is the peak frequency of the spectral profile, compensated with the frequency shift, $\hat{\theta}_l$. The *fibrillation amplitude*, a_l, is the amplitude shift, $\hat{a}_l$, of the spectral profile.

The shape of the fibrillation waves can be described by the harmonics of the fibrillation frequency. One approach is to employ the spectral line model, being a parametric representation of the spectral profile, ϕ_l, at its harmonics,

$$\phi_l(p_l + h_m) = \begin{cases} b_l e^{-\gamma_l m}, & m = 0, 1, \ldots, M \\ 0, & \text{otherwise,} \end{cases} \tag{8}$$

where b_l is the peak amplitude of the fundamental frequency, and γ_l is the *exponential decay* of the M harmonics; M is chosen so that only harmonics below 20 Hz are used. The parameter h_m denotes the offset position of the m:th harmonic in relation to the fundamental frequency at p_l. Estimators of the peak amplitude, $\hat{b}_l$, and the exponential decay, $\hat{\gamma}_l$, can be obtained by minimizing the least square error between the logarithm of the of the spectral line model and the logarithm of the spectral profile [6].

The parameters f_l, a_l, and γ_l are obtained each second from overlapping frames of 128 samples (i.e. 2.56 seconds at 50 Hz sampling rate). The parameter average and variation during the entire recording can therefore be calculated by simply using the mean and standard deviation.

2.3. Validity

The residual ECG signals are sometimes extremely noisy, and occasional episodes of sinus rhythm may be included. Therefore, it is necessary to exclude such segments from further analysis. To determine if the l:th segment contains AF, measures derived from the spectral profile, such as position and amplitude of the second largest peak and the amplitude of the noise, i.e., between the harmonics, are employed. Sudden changes in the residual ECG, possibly due to episodes of noise or sinus rhythm, are reflected by a suddenly increased model error. The ECG signal is considered to be valid, i.e., with atrial activity, if the relative amplitude of the spectral peak and its harmonics is sufficiently large, the second peak has neither to high amplitude nor is to close to the position of the fundamental frequency, and the model error has not suddenly increased [7].

2.4. Database

The database was provided by Physionet for use in the Computers in Cardiology Challenge 2004, and consists of 80 different two-channel ECG recordings. One minute segments were extracted from 20–24 hour Holter recordings from patients with paroxysmal AF (128 samples per second, 16 bits/sample, 200 A/D units per millivolt). The recordings have been divided into a training set and two test sets (A and B).

The 30 recordings of the training set were labeled either non-terminating (N), immediately-terminating (T), or soon-terminating (S). Ten recordings were labeled N, meaning that the AF episode continues at least one hour after the end of the recording. Twenty recordings from ten different patients were labeled S or T, where the T recording immediately follows the S recording. The AF episode terminates within one second of the end of the T

recording and, consequently, one minute after the end of the S recording.

Test set A contains 30 recordings from the same number of patients. The labels of the recordings are concealed, but it is known that approximately half of the recordings are labeled N and half T. Test set B contains 20 recordings, one labeled S and one labeled T from each of ten patients. The patient number and the labels of the 20 recordings are concealed.

The signals are resampled to 50 Hz, and the lead with most valid segments is considered for further analyses.

3. Results

Once occasional episodes of sinus rhythm and local noise have been excluded using the validity parameter, the parameters of the remaining segments are averaged. This produces reliable estimates of the mean fibrillation frequency, f, the exponential decay, γ, and the fibrillation amplitude, a. The variation of the fibrillation frequency, σ_f, is obtained using the standard deviation of the fibrillation frequency. In one of the signals of the training set, 6N, more than 75% of the segments were considered invalid and, therefore, the entire signal was excluded from further analysis.

Studying the residual ECG signals of the training set, we found that terminating AF generally exhibits a lower and more regular fibrillation frequency than does non-terminating AF. A sawtooth-like waveform of the fibrillation waves has larger harmonics, which results in a small value of γ, while a more sinus-wave-like waveform has smaller harmonics, which results in a larger value of γ, see Figure 2. Non-terminating AF generally has a larger exponential decay than does terminating AF. The mean and standard deviation of each parameter among the non-terminating (N) and the terminating (T) AF recordings of the training set are shown in Table 1. A two-sample Kolmogorov-Smirnov goodness-of-fit hypothesis test was employed to determine whether there was any difference in the parameter between the N and T signals. The asymptotic p-value implies that the fibrillation frequency, f, the exponential decay, γ, and the variation of the fibrillation frequency, σ_f, differ significantly between non-terminating and terminating AF.

No significant differences exist in any parameter of the averaged values between the S and the T recordings. Hence, to distinguish S from T recordings, a dynamic analysis was performed, revealing that the fibrillation frequency is slightly lower in the last seconds of the T recordings than for the S recordings. However, this difference is not statistically significant, since the difference among different recordings is large. Consequently, we compared the parameters of the last segment, i.e., 2.56 seconds, in the

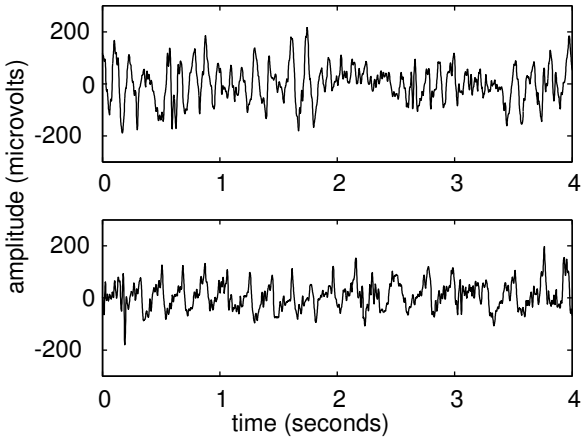

Figure 2. Residual ECGs with different exponential decay, γ. (a) Non-terminating AF with $\gamma = 1.6$ ($f = 7.6$ Hz, $\sigma_f = 0.9$), and (b) terminating AF with $\gamma = 0.7$ ($f = 5.0$ Hz, $\sigma_f = 0.4$).

Table 1. Mean value and standard deviation of the parameters used for AF characterization, from the non-terminating (N) and immediately-terminating (T) signals in the training set. The parameters with boldface asymptotic p-values are significantly different according to the Kolmogorov-Smirnov test.

Parameter average	N Mean $\pm$ Std	T Mean $\pm$ Std	p-value
f	6.91 ± 0.66	5.00 ± 0.65	**0.000033**
γ	1.29 ± 0.27	0.79 ± 0.20	**0.0021**
σ_f	0.80 ± 0.23	0.52 ± 0.13	**0.0127**
a	21.7 ± 12.4	28.6 ± 16.7	N.S.

S and T recordings from the same patient. The differences between the parameters of the last second in the S and T recordings are shown in Table 2. The Kolmogorov-Smirnov test shows that the fibrillation frequency is significantly lower in the last seconds of the T recording, than in the last seconds of the S recording.

Since there is significant correlation between the most significant parameter, i.e. the fibrillation frequency, f, and the other statistically significant parameters (γ: $r = 0.9$, $p < 0.0001$ and σ_f: $r = 0.5$, $p < 0.05$), only the fibrillation frequency was used for classification. The recordings of the training set and test set A were classified as non-terminating (N) if their average fibrillation frequency exceeded 5.7 Hz, and terminating (T) AF otherwise. The recordings of the training set were classified in pairs, where the recording with the highest fibrillation frequency in the last seconds for each recording was classified as soon-terminating (S) and the other recording as immediately-terminating (T).

Table 2. Mean value and standard deviation of the differences between the last segment in the immediately-terminating (T) and the soon-terminating (S) AF signal from a patient in the training set. The fibrillation frequency f differs significantly according to the Kolmogorov-Smirnov test.

Parameter last segment	S-T Mean $\pm$ Std	p-value
f_N	0.90 ± 1.02	**0.0239**
γ_N	-0.03 ± 0.21	N.S.
a_N	1.1 ± 13.4	N.S.

Table 3. Classification of recordings in the training set and test set into non-terminating (N) versus terminating (T) AF, and soon-terminating (S) versus immediately-terminating (T) AF.

	N and T	S and T
Training set	**19/20**	**16/20**
Test set	**27/30**	14/20

Since no information was provided about which recordings of test set B belong to the same patient, and there is limited practical clinical use for an automatic signal-pairing software, the recordings were paired manually. Just as with the training set, the signal with the highest fibrillation frequency in the last seconds in each pair was classified as S, while the other signal was classified as T. The classification results are presented in Table 3.

4. Discussion and conclusions

Predicting patients prone to spontaneous AF termination from Holter ECG recordings can be done with good accuracy (90%). A low and stable fibrillation frequency and a low exponential decay of the spectral profile are good indicators of spontaneous termination. Although the value of this study is limited by its small sample size, classifying the signals into terminating and non-terminating AF using only their fibrillation frequency works well. The idea that fibrillatory frequency may predict spontaneous [8],[9] or drug-induced AF termination [8],[10] has previously been advocated by our group. Additional parameters, such as exponential decay, may be included to classify the signals of a larger database.

In patients prone to spontaneous termination, an episode of AF is more likely to terminate spontaneously when the fibrillation frequency is lower. Therefore, it is possible to classify recordings from one patient into soon-terminating and immediately-terminating, based on the fibrillation frequency of the last seconds in the recording. However, in this database the fibrillation frequency often reaches its lowest value somewhere in the middle of the recordings. In addition to this, inter-patient differences are substantial. Therefore, it seems unlikely that the termination of AF can be predicted in general with high accuracy.

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