Medical Engineering & Physics 35 (2013) 668–675

Contents lists available at SciVerse ScienceDirect

Medical Engineering & Physics

journal homepage: www.elsevier.com/locate/medengphy

Predicting atrial fibrillation inducibility in a canine model by multi-threshold spectra of the recurrence complex network

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ARTICLE INFO

Article history:
Received 10 November 2011
Received in revised form 19 July 2012
Accepted 21 July 2012

Keywords:
Atrial fibrillation
Spectra analysis
Multi-threshold
Recurrence complex network
Postoperative evaluation

ABSTRACT

The purpose of this study is to predict atrial fibrillation (AF) from epicardial signals by investigating the recurrence property of atrial activity dynamic system before AF. A novel scheme is proposed to predict AF by using multi-threshold spectra of the recurrence complex network. Firstly, epicardial signals are transformed into the recurrence complex network to quantify structural properties of the recurrence in the phase space. Spectral parameters with multi-threshold are used to characterize the global structure of the network. Then the feature sequential forward searching algorithm and mutual information based Maximum Relevance Minimum Redundancy criterion are used to find the optimal feature set. Finally, a support vector machine is used to predict the occurrence of AF. This method is assessed on the pre-AF epicardial signals of canine which includes the normal group A (no further AF will happen), the mild group B (the following AF time is less than 180 s) and the severe group C (the following AF time is more than 180 s). 25 optimal features are selected out of 180 features from each sample. With these features, sensitivity, specificity and accuracy are 99.40%, 99.70% and 99.60%, respectively, which are the best among the recurrence based methods. The results suggest that the proposed method can predict AF accurately and thus can be prospectively used in the postoperative evaluation.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in clinical practice, which is characterized by rapid and uncoordinated atrial activation [1]. As an independent risk factor of stroke and embolism [2], patients with AF commonly show symptoms including palpitations, dizziness, fainting, fatigue and chest pain. Except for high morbidity, AF significantly reduces the quality of life and results in death [3]. According to the epidemiological data, approximately 2.3 million Americans and 4.5 million Europeans are suffering from AF [3,4]. Moreover, the prevalence of AF is no less than 10 million in China [5]. Practically, AF occurs mostly in elder people and happens more in men than in women. About 80% of individuals with AF are over 65 years old [6,7]. With population aging, it is likely to become a serious public health problem. Therefore, the diagnosis and the treatment of AF are of great important.

In clinical practice, the main therapies for AF are the pharmacotherapy and the ablation therapy [8]. The pharmacotherapy focuses on the rate control or rhythm control to keep the normal supply of blood. It cannot guarantee a cure and has many side effects [9]. Patients failing in anti-arrhythmic should be considered for ablation. Recently, the ablation has been proved to be an efficient therapeutic procedure for AF by isolation of the pulmonary veins or other foci. However, the success ratio of the operation is still far from satisfactory. Incomplete ablation lines often lead to recurrences of AF [10,11]. It is known that AF is often paroxysmal initially and becomes self-sustained with the time [12]. The postoperative evaluation (POE) of AF operation is great important, since the effective and timely treatment should be taken to prevent AF from recurring.

AF intrigues a wide range of research interest, but most of them are related with the detection of AF event, the prediction of AF termination, the propagation analysis and so forth [13–15]. Rare attention has been paid to the postoperative evaluation. In fact, the atrial electricity system may change during the transition between AF and normal sinus rhythm (NSR) [16,17]. It means that we can predict the recurrence of AF with an appropriate method, and manage it timely. However, previous studies did not cover it. Lovett and Ropella [16] proposed a time-frequency coherence estimator to study the changes during the conversion from AF to NSR. Recently, a strategy provided by Huang et al. [17] mentioned that they can detect the transition between AF and NSR based on RR intervals. In essence, those algorithms are based on AF signals, and can be only used to detect the initiation or termination of an AF event. Up to now, no effective method has been proposed to predict AF. To

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http://dx.doi.org/10.1016/j.medengphy.2012.07.012

make the analysis method usable for the postoperative evaluation, we propose the motif analysis of the complex network to quantify the atrial electrical activity dynamical structure in Ref. [18]. However, the motif analysis has the problem in distinguishing the paroxysmal AF and the persistent AF, since it describes the network with the local structure but loses the global structure. In order to characterize the behaviors underlying the atrial electrical dynamics, it is necessary to take into account the global structure of the complex network.

In this paper, the multi-thresholds spectra of the complex network are proposed to analyze the atrial electrical time series, which is closely related with the global topology. A novel idea of multi-threshold is firstly applied to eliminate the influence of the threshold. Then, a feature selection scheme is used to eliminate the redundancy and make much progress on the performance of the support vector machine. The data processing flow is shown in Fig. 1.

2. Methods

2.1. Spectra analysis of the recurrence complex network

In the last decade, the complex network becomes a popular method for the analysis of dynamical properties of real-world systems, including biological, climate networks and ecological community [19–21]. Among the algorithms of mapping time series into the complex networks, the recurrence complex network [22,23] may provide a unifying concept and practical framework for nonlinear time series by interpreting the adjacency matrix directly from the recurrence concept in the phase space.

As Donner et al. denoted in [22], the adjacency matrix $\mathbf{A}(\varepsilon)$ is a representation of recurrent states of a dynamical system in its n-dimensional phase space. Usually, the state vectors are reconstructed based on time series by using the time-delay embedding technique [24] with the embedding dimension n and the time delay t. In this case, owing to the multi-electrodes mapping system, we can obtain enough trajectories of the dynamical system under the study. Then, the state vector $\vec{x}_i$ can be defined as:

$$\vec{x}_i = \{x_i^1, x_i^2, \ldots, x_i^n\}, \quad i = 1, \ldots, N \tag{1}$$

where the state vector $\vec{x}_i$ is composed of n electrodes signals in the time i; x_i^n is the nth electrode signal in the time i; n is the number of the spatial distributed electrodes (the observing trajectories); N is the observing time, which defines a window on the trajectories of dynamic system under investigation: a lower value of N (a short window) focuses on small-scale recurrences, while a larger value of N (a long window) focuses on large-scale recurrences. The adjacency matrix $\mathbf{A}(\varepsilon)$ is defined as

$$\mathbf{A}_{i,j}(\varepsilon) = \Theta(\varepsilon - ||\vec{x}_i - \vec{x}_j||) - \delta_{i,j}, \quad i = 1, \ldots, N; \quad j = 1, \ldots, N \tag{2}$$

where $\Theta(\cdot)$ is the Heaviside function; $||\cdot||$ denotes the Euclidean norm in the considered phase space; $\delta_{i,j}$ is the Kronecker delta to avoid self-loop; ε is the distance threshold. According to the way that the recurrence complex network is built up, each state vector in the phase space is represented by one distinct node. Hence, the size of the network depends on the number of phase space vectors. Two states will be connected if their spatial distance is less than ε. No direction and weight is defined in the links.

Based on the recurrence complex network, the properties underlying the system can be investigated. Although many techniques (such as the degree distribution, the clustering coefficients, and the motif analysis) have been defined to acquire the structural properties of the networks, it is still far from understanding their global topological structure. In order to further characterize the networks, the spectra analysis which could provide global measures of the network properties was proposed in recent years [25–27]. The structure of the network may be completely described by the associated adjacency matrix. The adjacency matrix $\mathbf{A}$ with N nodes is an $N \times N$ matrix with elements $a_{i,j} = 1$ if the distance between the states $\vec{x}_i$ and $\vec{x}_j$ is less than ε. Apparently, the recurrence complex network is undirected and the matrix $\mathbf{A} = \mathbf{A}^{\mathrm{T}}$ is a real symmetric matrix. The matrix $\mathbf{A}$ has N real eigenvalues, in which $\lambda_N > \lambda_{N-1} > \cdots > \lambda_1$.

The spectra density $\rho(\lambda)$ and the moment of k order M_k is defined by Eqs. (3) and (4), respectively.

$$\rho(\lambda) = \frac{1}{N}\sum_{i=1}^{N}\delta_\mu(\lambda - \lambda_i) \tag{3}$$

$$M_k = \int_{-\infty}^{+\infty} \lambda^k \rho(\lambda) d\lambda \tag{4}$$

where λ_i is the eigenvalue of the adjacency matrix; N is the node number; $\delta_\mu(x)$ is a smoothed delta function. According to the theory of matrix eigenvalue, M_k is a useful quantified value of matrix which depicts the structure of the network. It can be calculated as follows:

$$M_k = \frac{1}{N}\sum_{i=1}^{N}(\lambda_i)^k \tag{5}$$

In the case of the dendritic structure, the odd order value of moment equals to zero, while it is much greater than zero when the loop and component (group) arise [28,29].

The quantitative characteristics of the recurrence networks depend on the threshold, which is of particular importance for the global network measurement. The value of ε should be chosen appropriately. If ε is too large, almost every state vector is a neighbor of other states and leads to many artifacts. On the other hand, a small ε causes few states in the recurrence plot, and thus we cannot learn anything about the structure of the underlying system. Traditionally, ε is selected to be 5% of the standard deviation of time series [22]. However, this may distort existing structure in the network and is not suitable for the noisy situation. We propose a novel concept of multi-threshold. First, ε_0 is chosen as the 5% of the standard deviation of time series. Then a set of thresholds is obtained by extending ε_0 to its two sides:

$$\boldsymbol{\varepsilon} = \{\varepsilon_0 - (m-1)\Delta, \ldots, \varepsilon_0 - \Delta, \varepsilon_0, \varepsilon_0 + \Delta, \ldots, \varepsilon_0 + m\Delta\} \tag{6}$$

Here the optimal value of m and Δ can be obtained by the following considerations. (1) To reduce the computation load, m should not be too big. (2) The value of Δ is determined by the time series itself. If the signals change sharply, the Δ should be small so as to catch more structure of the underlying system. In this paper, we empirically choose $m = 30$ and $\Delta = 0.0005$. The multi-threshold can catch the useful structures of the dataset missed by other threshold chosen methods. Consequently, the multi-threshold parameters can characterize the network efficiently. Since the loop and component (group) structures appear more than the dendritic structure in the complex network of observing dynamic system, the third and fifth order of the moment which depict the group structures are selected as spectral features. In addition, the second order of the moment is selected because it contains the most energy of the network. Therefore, three spectral features are calculated in this paper, which are the second, third and fifth order of the moment. Then, $2m \times 3$ features are obtained for each sample.

2.2. Feature selection method

For each of the signal segments, a vector of $6m$ features is calculated based on the structure and quantification of the network. However, such a high-dimensional space is not suitable for