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Searching for “order” in atrial fibrillation using electrogram morphology recurrence plots

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ABSTRACT

Background: Bipolar electrograms recorded during atrial fibrillation (AF) can have an appearance of chaotic/random behavior. The aim of this study was to use a novel electrogram morphology recurrence (EMR) analysis to quantify the level of order in the morphology patterns in AF.
Methods: Rapid atrial pacing was performed in seven dogs at 600 bpm for 3 weeks leading to sustained AF. Open chest high density electrical recordings were made in multiple atrial sites. EMR plots of bipolar electrograms at each site were created by cross-correlating morphologies of each detected activations with morphologies of every other activation. The following features of the EMR plots were quantified: recurrence rate (RR), determinism (DET), laminarity (LAM), average diagonal line length (L), trapping time (TT), divergence (DIV), and Shannon's entropy (ENTR). For each recording site, these measures were calculated for the normal sequence of morphologies and also after random shuffling of the electrogram orders.
Results: Electrograms recordings from a total of 3961 sites had average cycle lengths of 104 ± 22 ms resulting in an average of 100 ± 19 activations detected per 10-s recording and an average RR of 0.38 ± 0.28 (range 0.02–1.00). Shuffling the order of the activation morphologies resulted in significant decreases in DET, LAM, L, TT, and ENTR and significant increases in DIV.
Conclusions: EMR plots of AF electrograms show varying rates of recurrence with patterns that suggest an underlying deterministic structure to the activation sequences. A better understanding of AF dynamics could lead to improved methods in mapping and treating AF.

1. Introduction

Electrical activity during atrial fibrillation (AF) is characterized by complex activation patterns that are difficult to interpret. This includes variable activation times and changing atrial electrogram amplitudes and morphologies giving the appearance, at times, of highly erratic baseline behavior. To elucidate the evolution of these patterns and their clinical relevance is a challenge. One suggested mechanism for sustained AF is multiple reentrant circuits that wander in the atria [1,2]. There also has been growing evidence that some of these rhythms are driven by stable sources in the atria [3–8]. These sources can be in the form of focal activation, rotors, or reentry patterns resulting in the complex fibrillatory activity seen in the rest of the atria. There is still much that is not understood about dynamical behavior of AF and its impact on AF electrograms.

The recurrence plot (RP) was invented and used by Eckmann et al. [9] as a means to visualize non-linear dynamical behavior. Eventually many investigators in diverse fields, such as physics, astronomy, biology, and economics, studied complex dynamical behavior not readily apparent from observed raw time series [10]. The plots were used to visualize a pattern representing the evolution of a sequence of points of some variable in one or a small number of dimensions and characterize its structure. The processes studied using RPs can be mathematical time series generated by computer solutions to linear and nonlinear differential equations or time series generated by real sequential processes occurring in nature.

We have recently adapted the recurrence quantification analysis designed for scalar and vector time series to study electrogram morphology recurrence (EMR) during AF [11]. We previously showed that mapping using EMR could be used to identify areas of rapid and repeatable electrogram morphologies in patients with persistent AF [11]. From this technique it was also observed that even sites with changing morphologies had noticeable patterns

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that were not random. The aim of this study was to quantify the features of EMR plots obtained from a canine model of AF using methods proposed by Zbilut et al. [12,13] and Marwan et al. [17] that have been previously used to quantify the visual structures observed in recurrence plots of scalar and vector time series.

2. Methods

2.1. Rapid atrial pacing model

Electrograms obtained from a canine rapid atrial pacing model of AF were used for this study. Previously published techniques were used to create this animal model in seven purpose-bred hound dogs weighing 25–35 kg [14]. Sterile surgery for pacemaker implantation was performed with endocardial pacing leads placed in the right atrial appendage (RAA). The pacemakers were programmed to pace at 600 bpm at four times the capture threshold for 2–3 weeks. The pacemaker was turned off prior to studying the dogs in sustained AF. This protocol conforms to the Guide for the Care and Use of Laboratory Animals published by the U.S. National Institutes of Health (NIH Publication No. 85-23, revised 1996) and was approved by the Animal Care and Use Committee of Northwestern University.

2.2. Electrogram mapping protocol

Electrograms during spontaneous AF were obtained during an open chest study performed via a lateral thoracotomy [15]. A Unemap electrical mapping system (UnEmap, Auckland, New Zealand) was used to record bipolar electrograms from a triangular-shaped high density plaque with 130 electrodes. The electrodes were equally spaced (2 mm) and allowed 117 simultaneous bipolar electrograms to be obtained in each recording. Recordings were sequentially obtained from the anterior portion of the left atrial appendage (LAA), superior portion of the posterior left atrium between the left and right pulmonary veins bordering the left atrial roof (PLA1), mid portion of the posterior left atrium between the four pulmonary veins (PLA2), the anterior portion of the RAA, and the free wall of the lateral right atrium (RAFW). The left and right atrial sites were chosen to provide a diverse representation of AF electrogram characteristics. The posterior left atrium and pulmonary veins are known regions that are important for AF maintenance. The appendages are known locations for more organized atrial activity. There are known left and right atrial differences in activation rate. Ten seconds of data were obtained at each site.

2.3. Morphology recurrence plots

The principle for morphology recurrence analysis is illustrated in Fig. 1. Here, the recurrence pattern of the famous tongue twister "PETER PIPER PICKED A PECK OF PICKLED PEPPERS" is used as an example. The grid shown in Fig. 1 represents the recurrence plot with the text phrase on both the x and y axes. The square is colored black if the letter on the *x*-axis matches the letter or space on the *y*-axis that it intersects with and colored white if the letters or spaces do not match. It can be noted that all the squares falling on the line of identity are colored black as each letter and space is matched with itself. All other black squares represent letters and spaces that recur in the phrase.

There are a couple features of the recurrence plots that can be observed which offer insight on the dynamical behavior of the system. In the example presented in Fig. 1, there are diagonal lines besides the line of identity that are present in the recurrence plot. These short diagonal lines occur when there is a recurrence of a sequence of letters. For example, the sequence "_PICK" occurs twice

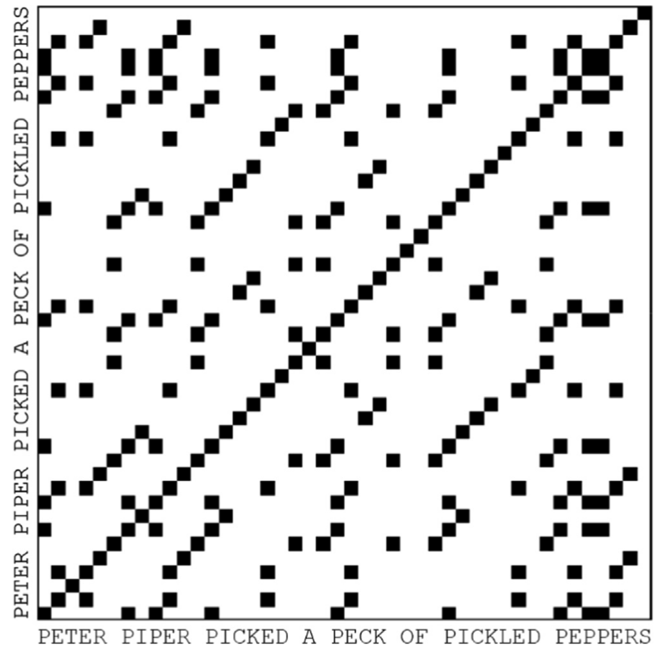

Fig. 1. Illustration of a recurrence plot using a well-known tongue twister. Black squares represent recurrences or points where letters on the *x* and *y* axes match.

in the tongue twister as does "ER_PI", both of which result in 5-point diagonal lines where the two occurrences meet on the *x* and *y* axes. Systems that have recurrences in sequences that results in diagonal lines have been described as having "deterministic" behavior. Additionally, recurrence plots can have vertical (and horizontal) lines that represent repetitive elements in the sequence. In Fig. 1, the double "P" in the word "PEPPERS" result in vertical lines with length of 2. Systems that have repetitive elements that result in vertical lines have been described as having "stationarity".

Recurrence plots for electrogram morphology can be created in a similar fashion to the text example in Fig. 1. Detecting recurrences in morphology of activation waveforms first requires robust detection of activation. This was accomplished using a previously validated cycle length iteration technique. Each activation waveform was defined as a 100-ms segment centered at the point of detection. As previously described [11], the morphology recurrence plot was generated by calculation of the cross-correlation coefficient of each electrogram to all other electrograms and plotted on a grid as indicated in Fig. 2. For the present analysis, whether morphologies of two different activation waveforms matched were determined if the cross-correlation coefficient was greater than the threshold $(1-\varepsilon)$. Fig. 2 illustrates the process of creating a morphology recurrence plot from an electrogram signal. The top of the figure shows an AF bipolar electrogram consisting of 13 discrete activations. These 13 activation waveforms were compared with each other with cross-correlation. The color-coded plot displays the cross-correlation coefficients for every combination of the activation waveforms. The black and white plot is a thresholded recurrence plot which identifies the pairs of activations that have cross-correlation coefficients greater than the $(1-\varepsilon)$ threshold, where $\varepsilon=0.2$. If the electrogram recording only contains electrograms with very similar morphology, a recurrence plot that is completely black would be expected.

2.4. Embedding dimension

As determinism and stationarity are the key features to gleaned from the recurrence plot, one of the ways to emphasize these elements over sporadic single point recurrences due to chance or