Feasibility of Nonlinear Heart Rate Variability Analysis in Clinical Settings

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Abstract

The measure of heart rate variability (HRV) has become a valuable metric for diagnosing cardiac health. The ECG is the representative signal containing information about the condition of this health metric. Analysis of this highly complex and irregular signal cannot always be addressed through linear statistics. Nonlinear methods are able to describe the processes generated by biological systems in a more effective way. The adoption of these methods in a clinical environment, however, has been difficult and slow. This paper examines the feasibility of using nonlinear analysis methods in such a setting. Given two data sets of a normal patient and a patient with atrial fibrillation (from PhysioNet), we examined the effectiveness of using Poincaré plots, largest Lyapunov exponent, and detrended fluctuation analysis, in differentiating the subjects. All the methods used were able to clearly separate the two data sets. From a clinical perspective, calculating accurate Lyapunov exponents requires an average of 5.5 hours of data, while Poincaré plots and DFA require approximately 100 and 80 minutes, respectively. Both Poincaré plots and DFA would serve well in characterizing a patient relatively quickly, while Lyapunov exponents would be too time intensive. To test our hypothesis, we designed and implemented a simple ECG system that gathered 90 minutes of data from an unclassified subject. A Poincaré and DFA analysis of the data suggested a healthy normal individual.

1 Introduction

It has been observed that the cyclic variations of heart rate plays an important role in the health of an individual. Heart rate variability (HRV), the variation over time of the period between heart beats, is thought to reflect the heart's ability to adapt to changing circumstances. Its variation may contain indicators of current diseases, or warnings about impending cardiac diseases. Physiological signals, however, often vary in a complex and irregular manner making it difficult to analyze them. Since the underlying mechanisms involved in the control of heart rate is mainly nonlinear [4], the application of nonlinear analysis techniques seem appropriate.

One of the controversial topics related to nonlinear science is the dynamical characterization of HRV. While the question as to whether the human heart is chaotic by nature is interesting, it is a question that is unlikely to be resolved very soon. Given the complexity of the human heart, where different subsystems with feedback loops constantly adapt the cardiac system to its physiological needs and requirements, it may very well be that the human heart is chaotic in one instance and stochastic in another. The debate as to its dynamic nature is interesting to the extent that it leads to new insights about health and disease in patients.

Setting aside the difficulties in documenting chaotic dynamics in HRV, the goal of this paper is to examine the feasibility of nonlinear analysis in a clinical setting. Towards that end, it examines several methods such as Poincaré plot analysis, Lyapunov exponents, and detrended fluctuation analysis (DFA) in distinguishing between groups of patients. Most studies of nonlinear techniques on

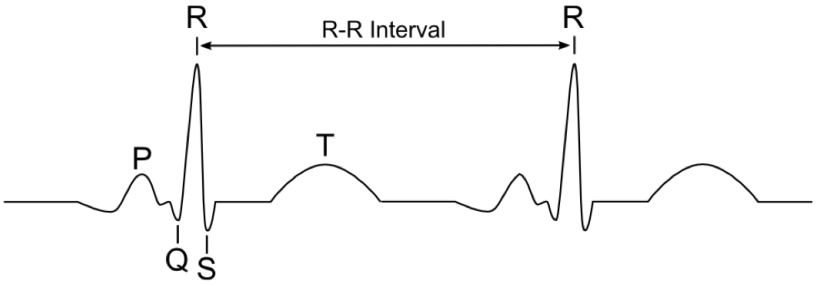

Figure 1: An ECG Example

HRV are based on long-term time series and hence focused on 24-hour ambulatory ECG recordings. We examine using these methods on consecutively smaller data lengths to determine their reliability in HRV classification.

Measuring the electrical impulses of the heart through an ECG is the standard way to study HRV. This paper examines 3 ECG data sets: a healthy subject, a subject with atrial fibrillation, and an unclassified subject. The first two data sets were obtained from PhysioNet, while the third was obtained experimentally through a custom ECG system. The length of time to obtain data from the third subject was informed by the results from the first two data sets. The third subject was then classified based on the analysis of the obtained ECG data.

In the next section, we describe the ECG data used and the RR interval method used in the analysis. Section 3 discusses in detail the nonlinear techniques used in characterizing the signals. The results of the analysis are provided in section 4. Section 5 presents the design and implementation of the custom ECG system followed by an analysis of the data obtained. We finally conclude in section 6.

2 ECG Data and Methods

An ECG measures the electrical impulses of heart activity, and is composed of four components: the p-wave, the QRS complex, and the t-wave (Figure 1). Typically, conditions of the heart are detected by irregular behavior in either the amplitude, duration, or frequency of the smaller waves or QRS complex. While they are valid methods for analysis, they require high resolution data and are affected by noise. Another alternative, which this paper explores, is to focus on the R-peak of the QRS complex, more specifically, the duration between the R spikes. This measure, dubbed the RR interval, is useful in detecting heart beat irregularities. It is robust to noise as it only requires keeping track of the time between major, easily detectable spikes. Given the RR intervals, the heart rate (beats per minute) is given as:

$$HR = 60/R_i \tag{1}$$

This paper analyses three data sets, two of which were obtained from the PhysioNet database of physiologic signals [2]. Each of the two time series from PhysioNet is 24 hours long. The first time series (n1rr) is of a healthy, adult male who is 32 years old. The second time series (a1rr) is of an atrial fibrillation (AF) patient. The sex, and age of the AF patient were not provided. The third data set was obtained experimentally, using a simple, custom ECG system, from a 30 year old adult male with no prior HRV classification (e.g.. normal, AF, cardiac arrhythmia, etc). Informed by our analysis of the two PhysioNet data sets, we gathered 90 minutes of ECG data and then used the data to classify the subject.

3 Nonlinear Methods of Analysis

Nonlinear techniques have been used in a variety of studies to describe complex biological systems in an effective way [1, 3]. The methods employed by this paper to study HRV include, interspike interval embedding, the largest Lyapunov exponent (LLE), Poincaré plot geometry, and detrended fluctuation analysis (DFA). Each is discussed in detail in the subsections below.

3.1 Poincaré Plots

A Poincaré plot analysis portrays the nature of RR interval fluctuations. It is a plot in which each RR interval is plotted as a function of the previous RR interval (RR_n against RR_{n+1}). It is used as a quantitative visual technique where the shape of the plot is used to indicate the degree of heart failure of the subject [10]. The plot provides summary information, as well as detailed beat-to-beat information on the behavior of the heart. It can be analyzed quantitatively by calculating the standard deviations of the distances of the $R - R(i)$ to the lines $y = x$ and $y = -x + (R - R_m)$, where $R - R_m$ is the mean of all the beat-to-beat intervals. The standard deviation of the short-term RR interval is referred to as SD1 (minor axis of the cloud), while the standard deviation of the long-term RR interval is called SD2 (major axis of the cloud). Typically, the ratio SD1/SD2 is used to characterize various cardiac abnormalities. A lower ratio is an indicator of a healthy heart and typically creates a comet or cigar-like plot.

3.2 Interspike Interval Embedding

Often, the first step in nonlinear dynamical analysis is the reconstruction of the phase space. It is used in calculating various measures such as the Lyapunov exponent (Section 3.3). The simplest method for reconstruction is the time-delay method described by Takens [8], where the multidimensional dynamics of the system can be generated from one measurement variable. In order for Takens theorem to hold, the sampling time interval needs to be uniform, which is not the case with RR intervals. If however, we assume that the spikes result from an integrate and fire process, then the RR_i(s) are just an integral of some state variable. This idea, proved by Sauer [7], allows the embedding of RR intervals using usual time delay embedding. The reconstructed and original system attractors are topologically equivalent. For a time series $R - R(n)$, where $n = 1, 2, ...N$, the time delay vectors in phase space can be reconstructed as defined by

$$X_n = [RR(n), RR(n + \tau), RR(n + 2\tau), ..., RR(n + (m - 1)\tau)] \tag{2}$$

where τ is referred to as the delay time and m is the embedding dimension. This paper employed the false nearest neighbors technique in estimating the embedding dimension, and the average mutual information technique in estimating the delay.

3.3 Largest Lyapunov Exponent (LLE)

The largest Lyapunov exponent is a quantitative measure of the sensitivity of the system to initial conditions and gives a measure of predictability. It defines the average rate of divergence of two neighboring trajectories. Even though an m-dimensional system has m Lyapunov exponents, it is often sufficient to compute just the largest Lyapunov exponent. A negative exponent implies that the orbits approach a common fixed point while a zero exponent represents orbits that maintain their relative positions (on a stable attractor). A positive exponent is indicative of orbits that are on a chaotic attractor. Different methods exist for calculating the largest Lyapunov exponent. The method employed by this paper was proposed by Rosenstein et al [6]. It is known to be robust with data length. This method looks for the nearest neighbor of each point in phase space and tracks their separation over a period of time. By plotting the log of the divergence versus time, the LLE is estimated by computing a least-squares fit to the linear region of the resulting curve. The LLE for normal subjects should be lower than patients diagnosed with AF since the variation in RR is much lower (compared to AF).

3.4 Detrended Fluctuation Analysis (DFA)

A time series is generally considered stationary if its mean, standard deviation and higher moments are invariant under time translation. Signals that fail these conditions are considered nonstationary. For such signals, a bounded time series can be integrated and mapped to a self-similar process. A sequence of coin flips, for example, can be mapped using this method to a one-dimensional random walk (a stationary integrated time series). However, using this type of fractal analysis for highly nonstationary signals like heart rate, only makes the nonstationary of the original data even more apparent during the integration procedure.

Detrended fluctuation analysis is used to overcome this complication. This technique, introduced by Peng et al [5], is a modified version of the root-mean-square analysis of a random walk that can be used to quantify the fractal scaling properties of short interval RR interval signals. The general idea behind DFA is to calculate the average amount of fluctuation over bins of different sizes (root mean square deviation between the signal and its trend in each bin) and plot the result as a function of bin size on a log-log scale.

First, the RR time series of length K is integrated using the equation,

$$y(k) = \sum_{i=1}^{k} [RR(i) - RR_{avg}] \tag{3}$$

where $y(k)$ is the kth value in the integrated series. $RR(i)$ is the ith interbeat interval and RR_{avg} is the average interbeat interval over the entire beat series. The integrated series is then divided in n windows of equal length. In each window, a least squares line representing the trend in that window is fitted to the RR interval data. The y coordinate of the straight line segments are denoted by $y_n(k)$. Finally, the integrated time series is detrended in each window. The root-mean-square fluctuation of the integrated and detrended series is calculated using equation 4.

$$F(n) = \sqrt{1/N \sum_{k=1}^{N} [y(k) - y_n(k)]^2} \tag{4}$$

This computation is repeated over different window sizes to obtain the relationship between $F(n)$ and the window size n. This relationship can be thought of as the number of beats in a window that is the size of the window of observation. Usually, $F(n)$ will increase with window size. A linear relationship on a log-log graph indicates the presence of self-similarity. The fluctuations in small boxes are related to the fluctuations in large boxes in a power-law fashion. The slope of the line, relating $\log F(n)$ to $\log n$ determines the scaling exponent, α. Fractal like signals result in a scaling exponent value of 1 ($\alpha = 1$). A totally random signal results in a value of 0.5. For a more intuitive understanding, α can be thought of as the "coarseness" of the original time series. The larger the value of α, the smoother the series.

For healthy, normal subjects, the scaling exponent should be closer to 1, indicating fractal-like behavior. For highly varying signals, like patients with atrial fibrillation, the exponent should be very low [9].

4 Results

Using the nonlinear methods discussed above, the two data sets for normal and AF subjects were analyzed. The results focus on the feasibility of using nonlinear approaches in analyzing cardiovascular variability in a clinical setting. If, for example, 24 hours of ECG data is required for a particular nonlinear analysis method, it would be too time intensive to succeed in a clinical environment.

Figure 2 shows the Poincaré plots for both subjects. For the normal subject, the classic cigar shape is clearly visible in the plot. The ratio SD1/SD2 for the normal subject is 0.85. In the case of the AF subject, the plot shows a "fan-like" dispersion. The ratio SD1/SD2 for the AF subject is 3.02, indicative of an unhealthy heart. This ratio is more in the case of the AF subject due to more

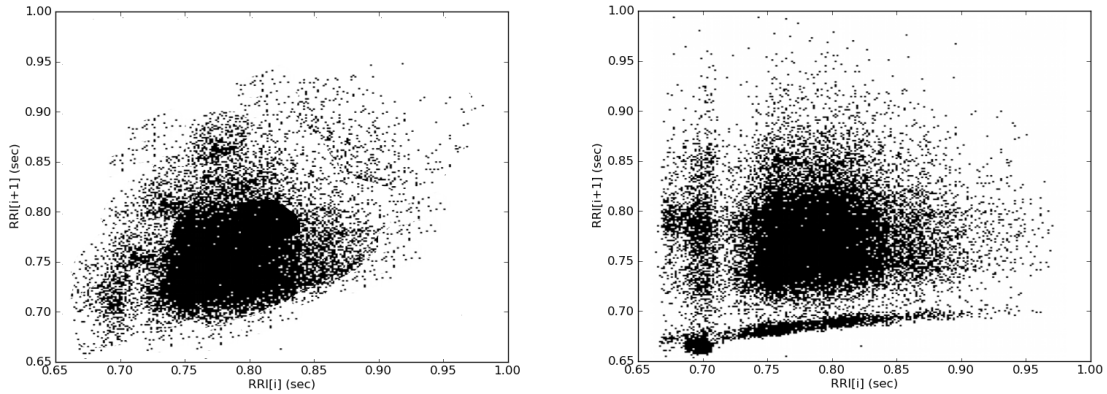

Figure 2: Poincaré plots for normal subject (left) and AF subject (right). The SD1/SD2 ratios are 0.85 and 3.02 respectively.

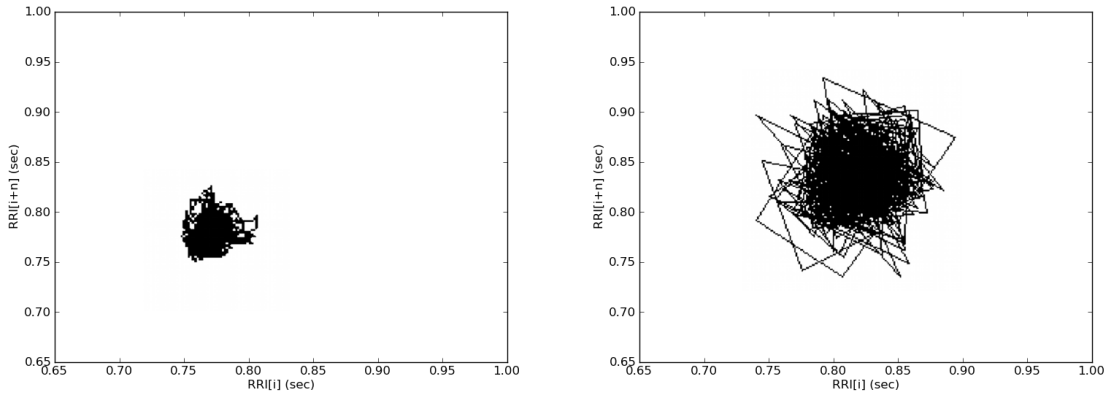

Figure 3: Phase-space plots for normal subject (left, $m = 7$, $\tau = 2$) and AF subject (right, $m = 8$, $\tau = 2$).

variation in the RR interval. The Poincaré plots, differentiates the two data sets significantly. To get a clear picture of the plots, approximately 10000 ($\sim$ 1.5hrs) beats were required.

To generate the phase-space plots, Tisean was used to compute the embedding dimension (m) and the delay (τ). The embedding dimension was calculated using false nearest neighbors and the delay was estimated using average mutual information. Figure 3 details the phase-space plots for the two data sets. For the normal subject, the phase-space plot looks like a cluster of points. In the case of atrial fibrillation, heart rate signal records highly erratic variability; this is depicted in the scattering of points in the phase-space plot.

Given a reconstruction of the phase space, the LLEs for the normal and AF subjects were calculated (using Tisean lyap_r). In order to determine the minimum amount of data required for a successful estimation, LLEs were calculated for different time lengths. Table 1 details the results. The LLEs computed from 20 hours of ECG data are the most accurate. Given this baseline, LLEs were then computed for progressively smaller data lengths. For the normal subject, an accurate LLE estimate can be obtained with 5 hours of ECG data; the AF subject required 6 hours. Results show a positive LLE for both data sets, suggesting a chaotic time series. While the LLE characterizes the two subjects well, with the AF subject having a higher LLE than the normal subject (due to higher RR variations), it is too time intensive for a clinical setting.

The last nonlinear method employed to distinguish the two data sets was DFA. Figure 4 shows

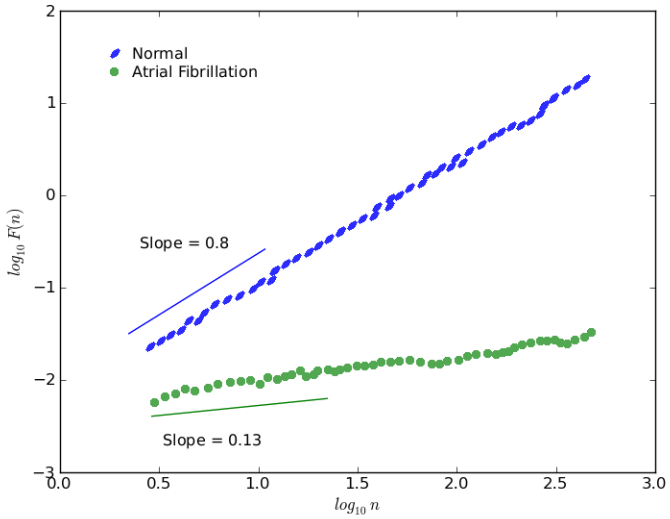

Figure 4: DFA analysis

the results of the analysis. For the normal subject, the fractal scaling (α) exponent is 0.8. In previous studies, healthy subjects revealed a scaling exponent of approximately 1 [9], indicating fractal-like behavior. For highly varying signals, like patients with AF, the scaling exponent is very low. The results support this conclusion with the AF subject having a reduced scaling exponent of 0.13. This method required approximately 8000 beats ($\sim$ 80min), the least amount of data out of the nonlinear methods used.

Table 1: LLEs for various time lengths

	Normal	AF
LLE (10 min)	0.03	0.09
LLE (1 hr)	0.23	0.43
LLE (3 hrs)	0.49	0.35
LLE (5 hrs)	**0.53**	0.45
LLE (6 hrs)	0.56	**0.66**
LLE (8 hrs)	0.57	0.64
LLE (20 hrs)	0.55	0.67

5 Experiment and Analysis

Of the nonlinear analysis methods used, Poincaré plot geometry, and DFA required the least amount of data for distinguishing the two subjects. While 1.5 hours of ECG data is still considerable, it is not as prohibitive as a 24 hour requirement. To test these two methods, a simple ECG system was developed and used to gather data from an unclassified subject. The experimental ECG system is by no means perfect, but since the analysis methods described above only require RR intervals, the system only needs to detect the spikes in the signal train and not the finer characteristics (p-wave and t-wave). The simple ECG designed for this experiment is different from many others in that it greatly simplifies the circuitry by eliminating noise reduction components, accomplishing this via software-based data post-processing.

The electrical signals generated by the heart can be detected on the surface of the skin. In theory one should be able to grab two leads of a standard voltmeter and see the voltage change with

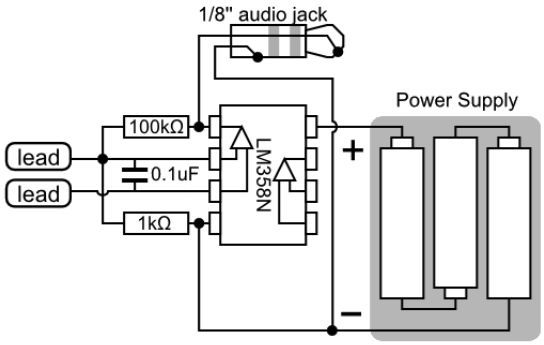

Figure 5: Simple ECG circuit

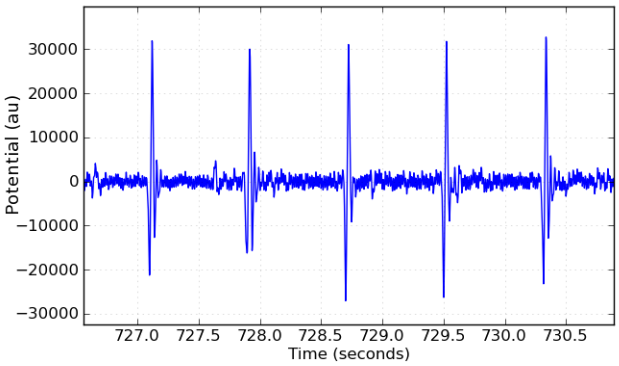

Figure 6: ECG signal of unclassified subject

each heart beat. However, since the fluctuations are rapid and the signal is extremely weak (a few millionths of a volt) by the time it reaches the skin, it is difficult to detect without amplification. A simple way to amplify the electrical difference between two points is via an operational amplifier. The gain on an op-amp is controlled by varying the resistors attached to it. Unfortunately, the amplifier also amplifies radiation from a variety of other electrical sources (computers, cell phones, lights, wiring) which is absorbed by the skin and is measured with the ECG. The traditional method for dealing with noise is complicated analog circuity. However, since the ECG signal is much slower in comparison to the characteristic, repeating, high-frequency noise, it can be separated using digital signal processing software on the computer. In order to digitize the signal, the analog to digital converter found in the common audio input of a computer sound card can be used.

The circuit diagram of the ECG system is detailed in Figure 5. The 0.1uF capacitor was used to stabilize the signal and reduce high frequency noise. With the circuit output connected to the audio input of the sound card, a sound editor was used to record the ECG data in live mode. Once the data was recorded, it was post processed by applying a lowpass filter at 30Hz. This eliminated most of the electrical noise (> 30Hz), while leaving the ECG intact (< 15Hz). Since, the low pass filter dramatically decreased the potential of the waveform, the volume of the signal was increased. Finally an auto-gain filter was employed to normalize the heart beat potentials.

The ECG signal of the unclassified subject can be seen in Figure 6. It is clear from the trace that even after processing there is still a lot of noise present. While the p-wave and the t-wave are lost in the noise, the R spike is clearly visible and the RR intervals can be calculated. A Poincaré plot of the RR intervals (Figure 7) of the subject seems to suggest a normal, healthy individual. The shape of the plot follows a "cigar-like" pattern and a quantitative analysis of the standard deviations reveals a low SD1/SD2 ratio of 0.77. This classification is confirmed by the DFA analysis, shown in

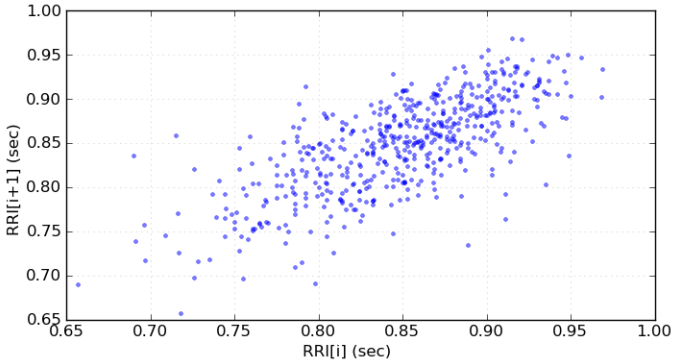

Figure 7: Poincaré plot of unclassified subject

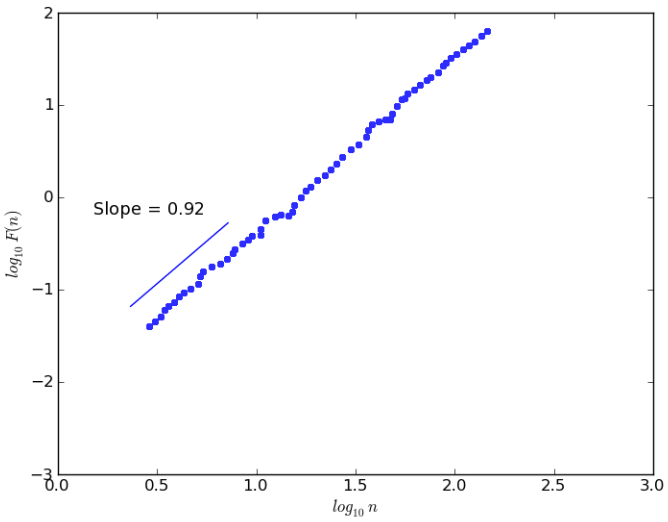

Figure 8: DFA analysis of unclassified subject

Figure 8, where the scaling exponent ($\alpha = 0.92$) is a value close to 1, indicating a healthy subject.

6 Conclusion

Methods from nonlinear dynamics provide valuable information regarding the dynamics and stucture of beat-to-beat time series. In this paper, we explored the feasibility of using nonlinear analysis methods in a clinical setting. More specifically, Poincaré plots, LLE, and DFA methods were used in analyzing HRV of two data sets (normal and AF) from PhysioNet. While our analysis allowed us to clearly differentiate the subjects, the data length required varied depending on the method used. Of the three methods used, calculating Lyapunov exponents required the most amount of data, with an average of 5.5 hours of data, while Poincaré plots and DFA required an average of 90 minutes of data. In a clinical setting, both Poincaré plots and DFA would serve well in characterizing a patient, while Lyapunov exponents would be too time intensive. To test our hypothesis, we designed and implemented a simple ECG circuit and gathered 90 minutes of data from an unclassified subject. A Poincaré and DFA analysis of the data suggests a healthy normal individual.

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