TIME SERIES ANALYSIS OF ECG SIGNALS SIMULATED FROM A MATHEMATICAL MODEL

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Abstract. *This article deals with time series analysis of the heart rhythm dynamics represented by electrocardiogram (ECG) signals. A mathematical model built upon three modified Van der Pol oscillators connected with time delay coupling are used to generate the ECG signals. Under this assumption, the heart dynamics is represented by a system of differential-difference equations and numerical simulations present results qualitatively coherent with real ECG signals. The analysis of normal and ventricular fibrillation signals generated from numerical simulations of the mathematical model are conducted. Concerning time series analysis, the method of delay coordinates are employed for the state space reconstruction and delay parameters are calculated from the method of average mutual information and the method of the false nearest neighbors. Lyapunov exponents are estimated employing the algorithm due to Kantz. Results establish the main dynamical characteristics of the heart rhythms identifying order and chaos from ECG signals.*

Keywords*: Heart, natural rhythms, ECG, nonlinear dynamics, chaos, time series, state space reconstruction.*

1. INTRODUCTION

Rhythmic changes of blood pressure, heart rate and other cardiovascular measures indicate the importance of dynamical aspects in the comprehension of cardiovascular rhythms. Several studies are pointing to the fact that certain cardiac arrhythmias are instances of chaos (Witkowski *et al.*, 1998; Radhakrishna *et al.*, 2000; Savi, 2005, 2006). This is important because it may suggest different therapeutic strategies, changing classical approaches. The clinical arrhythmias that have the greatest potential for therapeutic applications of chaos theory are the aperiodic tachyarrhythmias, including atrial and ventricular fibrillation. Garfinkel *et al.* (1992, 1995) discuss the application of chaos control techniques in order to avoid heart arrhythmic responses.

There are different forms to evaluate the heart functioning by the measurement of some signal and electrocardiogram (ECG) and tachogram are probably the most popular measurements. An electrocardiogram (ECG) records the electrical activity of the heart being used to measure the rate and regularity of heartbeats as well as the size and position of the chambers. The electrical impulses related to heart functioning are recorded in the form of waves, which represents the electrical current in different areas of the heart.

This article proposes a time series analysis from ECG signals generated from a mathematical model built by three coupled modified Van der Pol oscillators connected considering time delay coupling. This oscillator is very useful in the phenomenological modeling of the heartbeat since it displays many of those features supposed to occur in heart dynamics as limit cycle, synchronization and chaos. The heart dynamics is represented by a system of differential-difference equations and numerical simulations present results qualitatively coherent with ECG signals. Normal and ventricular fibrillation signals are analyzed establishing the main characteristics of the heart rhythms. In brief, normal ECG is related to regular response while fibrillation is associated with irregular response. Therefore, it is important to identify dynamical characteristics of both signals in order to think in terms of strategies to avoid fibrillation behavior. The method of delay coordinates is employed for the state space reconstruction. Delay parameters are calculated from the method of average mutual information and the method of the false nearest neighbors. Lyapunov exponents are estimated employing the algorithm due to Kantz (1994). Results from these three methods are based on TISEAN package (Hegger *et al.*, 1999). Although real ECG signals are always contaminated by noise, the developed analysis considers robust procedures that make the conclusions acceptable for real signals (Franca & Savi, 2001a,b, 2003). As conclusions, the time series analysis establishes the main dynamical characteristics of the system, indentifying order and chaos related to heart rhythms.

2. MATHEMATICAL MODEL

The normal cardiac rhythm is primarily generated by the SA node, which is considered as the normal pacemaker. Besides, the AV node is another pacemaker and each of these instances presents an actuation potential that is fundamental to the heart dynamics. These pacemakers are responsible for the P-curve and the QRS-complex is associated with the pulse propagation through the ventricles, which physiologically represents the His-Purkinje complex.

Under these assumptions, it is possible to model the heart dynamics by considering three coupled oscillators. Gois & Savi (2009) presents a novel model where bidirectional asymmetric couplings are assumed among all oscillators. Moreover, external excitations are incorporated to the system, considering a periodic driving term on each oscillator, $\Gamma_i(t)$. Figure 1 presents the conceptual model of the heart dynamics, indicating the three oscillators involved and the general connection among them. Since time delays in signal transmission are unavoidable, the proposed mathematical model is represented by a set of differential-difference equations as follows:

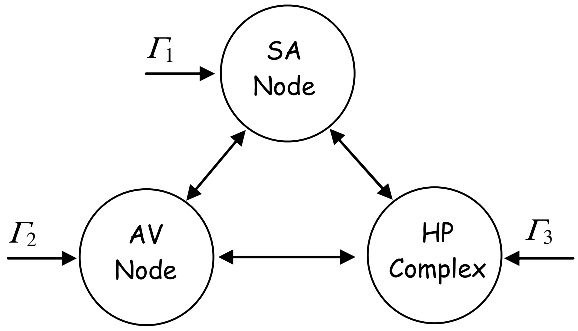

Figure 1. Conceptual model with three coupled oscillators.

$$
\begin{aligned}
&\dot{x}_1 = x_2 \\
&\dot{x}_2 = -a_{SA}x_2(x_1 - w_{SA_1})(x_1 - w_{SA_2}) - x_1(x_1 + d_{SA})(x_1 + e_{SA}) + \rho_{SA}\sin(\omega_{SA}t) + \\
&\qquad + k_{SA-AV}(x_1 - x_3^{\tau_{SA-AV}}) + k_{SA-HP}(x_1 - x_5^{\tau_{SA-HP}}) \\
&\dot{x}_3 = x_4 \\
&\dot{x}_4 = -a_{AV}x_4(x_3 - w_{AV_1})(x_3 - w_{AV_2}) - x_3(x_3 + d_{AV})(x_3 + e_{AV}) + \rho_{AV}\sin(\omega_{AV}t) + \\
&\qquad + k_{AV-SA}(x_3 - x_1^{\tau_{AV-SA}}) + k_{AV-HP}(x_3 - x_5^{\tau_{AV-HP}}) \\
&\dot{x}_5 = x_6 \\
&\dot{x}_6 = -a_{HP}x_6(x_5 - w_{HP_1})(x_5 - w_{HP_2}) - x_5(x_5 + d_{HP})(x_5 + e_{HP}) + \rho_{HP}\sin(\omega_{HP}t) + \\
&\qquad + k_{HP-SA}(x_5 - x_1^{\tau_{HP-SA}}) + k_{HP-AV}(x_5 - x_3^{\tau_{HP-AV}})
\end{aligned}
\tag{1}
$$

where $x_i^{\tau} = x_i(t-\tau)$ and τ represents the time delay. Notice that, actually, there are different delays depending on the connection type. The general idea of these coupled oscillators is that the ECG signal is built from the composition of these signals as follows:

$$X = ECG = \alpha_0 + \alpha_1 x_1 + \alpha_3 x_3 + \alpha_5 x_5 \tag{2}$$

Analogously, it is possible to define:

$$\dot{X} = \frac{d(ECG)}{dt} = \alpha_1 x_2 + \alpha_3 x_4 + \alpha_5 x_6 \tag{3}$$

Numerical procedure employed to deal with these differential-difference equations is an adapted fourth-order Runge-Kutta method. Basically, by considering the system $\ddot{y} = f(y, \dot{y}) + \Gamma(t) + K[y - y^{\tau}]$, it is assumed a function equivalent to the delayed system and, for time instants $t < \tau$, the function y_0 provides values corresponding to time delays prior to the initial instant of observation (Boucekkine *et al.*, 1997): $y_0(t) = y(t-\tau)$. The determination of $y_0(t)$ may be done using Taylor's series, approximating the exact solution as follows (Cunningham, 1954):

$$y(t-\tau) \cong y(t) - \tau\,\dot{y}(t) + \frac{\tau^2}{2}\ddot{y}(t) \tag{4}$$

Under this assumption, it is possible to obtain approximated values for $y(t-\tau)$ at least in the time interval $t < \tau$. After this, it is possible to use the integrated values in order to construct the time delayed function.

3. TIME SERIES ANALYSIS

The basic idea of the state space reconstruction is that a signal contains information about unobserved state variables that can be used to predict the present state. Therefore, a scalar time series, s_n, may be used to construct a vector time series that is equivalent to the original dynamics from a topological point of view (Savi, 2006). The state space reconstruction needs to form a coordinate system to capture the structure of orbits in state space, which could be done using lagged variables, $s_{n+\tau}$, where τ is the time delay. Then, it is possible to use a collection of time delays to create a vector in a D_e-dimensional space,

$$u(t) = \{s_n, s_{n+\tau}, \ldots, s_{n+(D_e-1)\tau}\}^T \tag{5}$$

The literature reports many methods employed to determine time delay, τ. The mutual information method (Fraser & Swinney, 1986) presents good results, which disseminate its use. The determination of embedding dimension, D_e, also involves different methods and the method of the false nearest neighbors (Kennel *et al.*, 1992) is a good alternative with this aim. Lyapunov exponents evaluate the sensitive dependence to initial conditions considering the exponential divergence of nearby orbits. Once again, there are a lot of procedures to estimate these exponents and the algorithm proposed by Kantz (1994) is an interesting alternative presenting robustness with respect to noise (Franca & Savi, 2003). Kantz & Schreiber (1997) presents a general overview of nonlinear time series analysis and the forthcoming sections present a brief discussion of these methods.

3.1 - Method of Average Mutual Information

Fraser & Swinney (1986) establishes that the time delay τ corresponds to the first local minimum of the average mutual information function $I(\tau)$, which is defined as follows,

$$I(\tau) = \sum_{n=1}^{N-\tau} P(s_n, s_{n+\tau}) \log_2 \left[\frac{P(s_n, s_{n+\tau})}{P(s_n)\, P(s_{n+\tau})} \right] \tag{6}$$

where $P(s_n)$ is the probability of the measure s_n, $P(s_{n+\tau})$ is the probability of the measure $s_{n+\tau}$, and $P(s_n, s_{n+\tau})$ is the joint probability of the measure of s_n and $s_{n+\tau}$. When the measures s_n and $s_{n+\tau}$ are completely independent, $I(\tau) = 0$. On the other hand, when s_n and $s_{n+\tau}$ are equal, $I(\tau)$ is maximum. Therefore, the analysis of the $I(\tau)$ curve allows one to determine the best time delay to be used in the state space reconstruction.

3.2 - Method of the False Nearest Neighbors

The method of the false nearest neighbors was originally developed for determining the number of time delay coordinates needed to recreate autonomous dynamics, but it is extended to examine the problem of determining the proper embedding dimension. In an embedding dimension that is too small to unfold the attractor, not all points that lie close to one another will be neighbors because of the dynamics. Some will actually be far from each other and simply appear as neighbors because the geometric structure of the attractor has been projected down onto a smaller space (Kennel *et al.*, 1992).

In order to use the method of the false nearest neighbors, a D-dimensional space is considered where the point u_n has r-th nearest neighbors, u_n^r. The square of the Euclidean distance between these points is,

$$r_D^2(n,r) = \sum_{k=0}^{D-1} \left[s_{n+k\tau} - s_{n+k\tau}^r \right]^2 \tag{7}$$

Now, going from dimension D to D+1 by time delay, there is a new coordinate system and, as a consequence, a new distance between u_n and u_n^r. When these distances change from one dimension to another, these are false neighbors. A proper space dimension may be obtained when there are no false neighbors after a dimension increase.

3.3 – Lyapunov Exponents

Lyapunov exponents evaluate the sensitive dependence to initial conditions considering the exponential divergence of nearby orbits. Therefore, it is necessary to evaluate how trajectories with nearby initial conditions diverge. The signs of the Lyapunov exponents provide a qualitative picture of the system's dynamics. The existence of positive Lyapunov exponents defines directions of local instabilities in the system dynamics (Franca & Savi, 2003).

The algorithm proposed by Kantz (1994) uses the same idea of the one proposed by Wolf *et al.* (1985) which considers the reconstructed attractor and examines orbital divergence on length scales, working in tangent space. The method monitors the long-term evolution of a single pair of nearby orbits and is able to estimate the non-negative Lyapunov exponents. Kantz (1994) considers that the divergence rate trajectories fluctuate along the trajectory, with the fluctuation given by the spectrum of effective Lyapunov exponents. The average of the effective Lyapunov exponent along the trajectory is the true Lyapunov exponent and the maximum value is given by

$$\lambda(t) = \lim_{\varepsilon \to 0} \frac{1}{\delta} \ln\left(\frac{|u(t+\delta) - u_{\varepsilon}(t+\delta)|}{\varepsilon} \right) \tag{8}$$

where $|u(0) - u_\varepsilon(0)| = \varepsilon$ and $u(t) - u_\varepsilon(t) = \varepsilon\, v_u(t)$, with $v_u(t)$ representing the eigenvectors associated with the maximum Lyapunov exponent, $\lambda_{\max}$; δ is a relative time referring to the time index of the point where the distance begin to be greater than ε, $\delta(0)$. This algorithm is not noise sensitive being a good alternative to time series analysis (Franca & Savi, 2003).

4. ECG ANALYSIS

This section considers time series analysis of the ECG signals generated by numerical simulation of the mathematical model here presented. The following parameters are adopted to represent the normal heart functioning: $a_{SA} = 3$, $w_{SA_1} = 0.2$, $w_{SA_2} = -1.9$, $d_{SA} = 3$, $e_{SA} = 4.9$; $a_{AV} = 3$, $w_{AV_1} = 0.1$, $w_{AV_2} = -0.1$, $d_{AV} = 3$, $e_{AV} = 3$; $a_{HP} = 5$, $w_{HP_1} = 1$, $w_{HP_2} = -1$, $d_{HP} = 3$, $e_{HP} = 7$, $\alpha_0 = 1, \alpha_1 = 0.1, \alpha_3 = 0.05, \alpha_5 = 0.4$. Concerning coupling aspects, it is assumed that the normal heart has a unidirectional coupling from SA to AV nodes and also from AV to HP. Therefore, $k_{SA\text{-}AV} = 5$ and $k_{AV\text{-}HP} = 20$ are non-vanishing terms and all other couplings vanishes. Moreover, it is necessary to establish proper coupling time delay parameters: $\tau_{SA\text{-}AV} = 0.8$ and $\tau_{AS\text{-}HP} = 0.1$, vanishing all others. For more details about system parameters, see Gois & Savi (2009).

Under this condition, the ECG simulation is carried out and the result is presented in Figure 2 together with a measured real signal. Notice that numerical simulation is in close agreement with the real ECG signal, capturing the general behavior of the real ECG measured at the second derivation. Essentially, the ECG presents a regular, periodic response. Since numerical simulations are in agreement with experimental tests they are used in time series analysis representing the real signal.

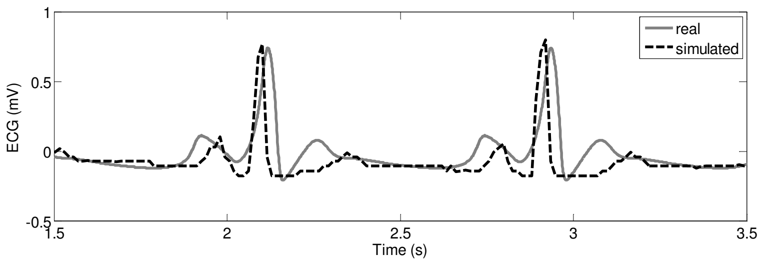

Figure 2. Real and simulated normal ECG comparison.

The normal ECG signal with 20,000 data points is used in order to perform the state space reconstruction. Initially, the delay parameters are analyzed by considering the mutual information and the false neighbor methods, as presented in Figure 3. Although the first minimum of the information curve is not clearly defined, it is used a global minimum of the first region defined by the first local maximum, pointing that time delay needs to be $\tau = 0.4$s. On the other hand, the analysis of the embedding dimension shows that there are no false neighbors for $D > 3$, and it is assumed that $D_e = 3$. Under these assumptions, the method of delay coordinate can be employed for the space reconstruction. Figure 4 presents a two-dimension projection of the reconstructed space together with the real one obtained from the numerical simulation, showing a good agreement in a topological point of view (Savi, 2006). The Lyapunov exponent estimation is done by considering the Kantz algorithm assuming different embedding dimension. This result is presented in Figure 5 showing that the slope of the curve vanishes, which means that the greatest exponent is null, confirming the regular characteristic of the normal ECG signal.

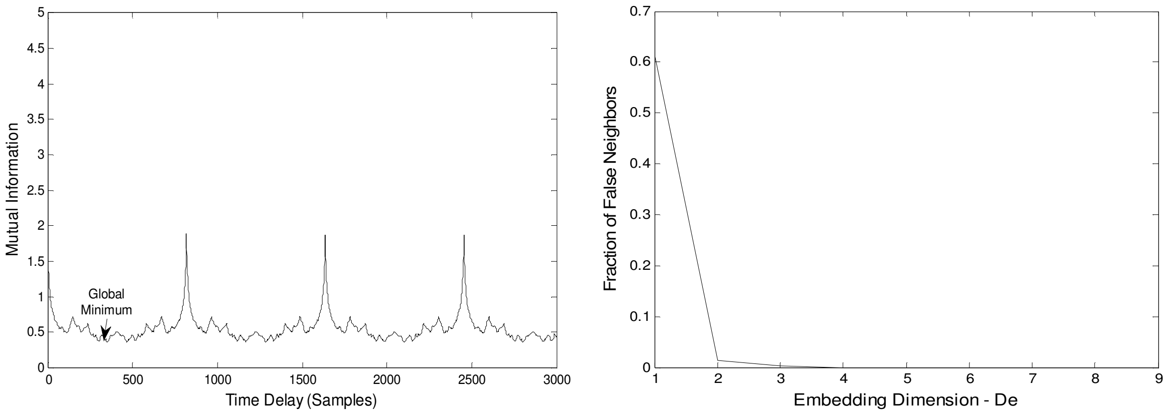

Figure 3. Delay parameter analysis for the normal ECG.

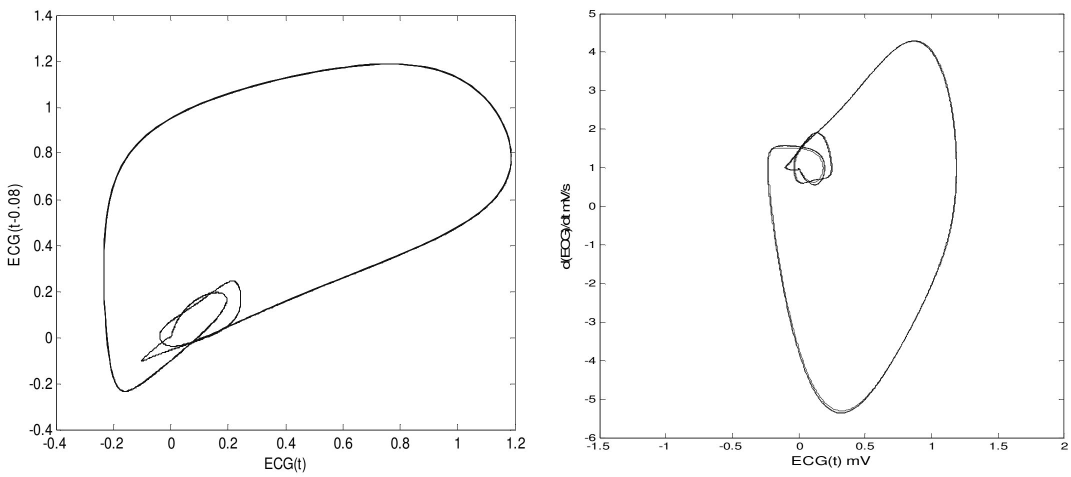

Figure 4. Normal ECG phase space using the heart-model: reconstructed from its output the time series (left) and traced direct from its states (right).

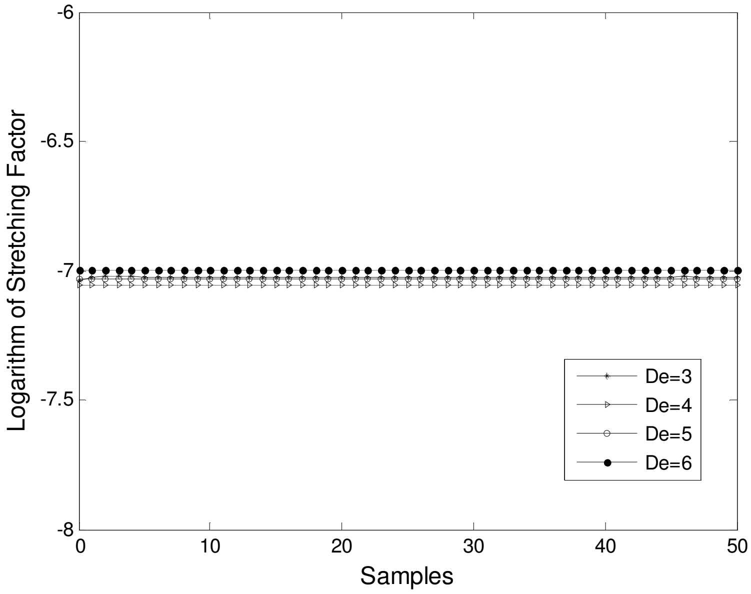

Figure 5. Lyapunov exponents for the normal ECG.

The forthcoming analysis is dedicated to the ventricular fibrillation ECG signal. This pathological behavior is simulated by considering the normal ECG parameters but that external pacemakers are exciting the heartbeat. Therefore, besides the previous parameters it is considered the following forcing parameters: $e_{SA} = 6$, $\rho_{SA} = 1$, $\rho_{AV} = 1$, $\rho_{HP} = 20$, $\omega_{SA} = \omega_{AV} = \omega_{HP} = 2\pi/(60/70)$. Figure 6 shows the numerical simulation and the real ECG related to this condition. Note a qualitative agreement between them showing that the model captures the general physiological behavior of ventricular fibrillation (Gois & Savi, 2009).

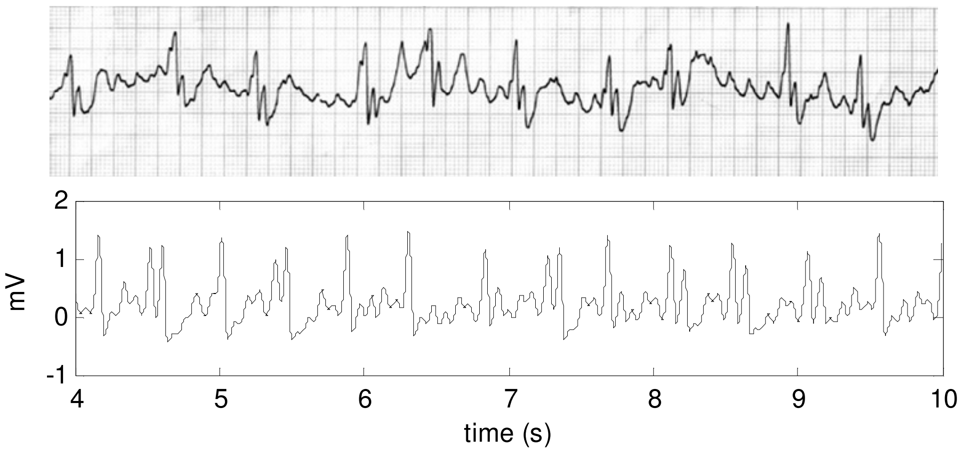

Figure 6. Ventricular fibrillation ECG (real, up; simulated, down).

This ventricular fibrillation ECG signal is now used to perform the state space reconstruction. Once again, a signal with 20,000 data points is used for the time series analysis. The delay parameter analysis is presented in Figure 7. As presented in the normal ECG, the first minimum of the mutual information curve is not clearly defined and the same procedure is employed allowing the determination of the time delay as $\tau = 0.100$s. On the other hand, the embedding dimension is assumed to be $D_e = 10$. This result shows the increase of the signal complexity that is expected by the physiological characteristic of the ventricular fibrillation. By employing these parameters, the method of delay coordinate can be used to perform the space reconstruction. Figure 8 presents different projection of the reconstructed space and all pictures point to a complex dynamics. Figure 9 presents the Lyapunov exponents evaluated from the Kantz algorithm assuming different values of the embedding dimension. This analysis shows that the greatest exponent is positive (λ=+0.2286), confirming that ventricular fibrillation is related to chaos.

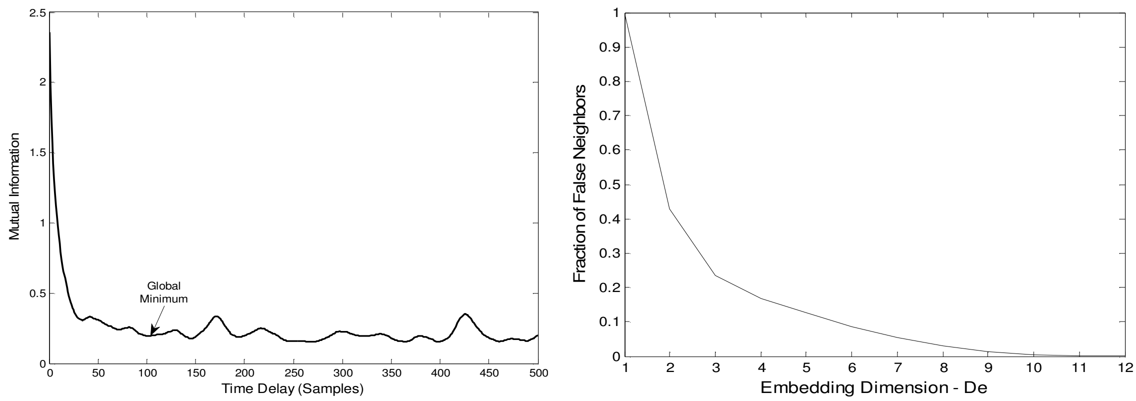

Figure 7. Delay parameter analysis for the ventricular fibrillation ECG.

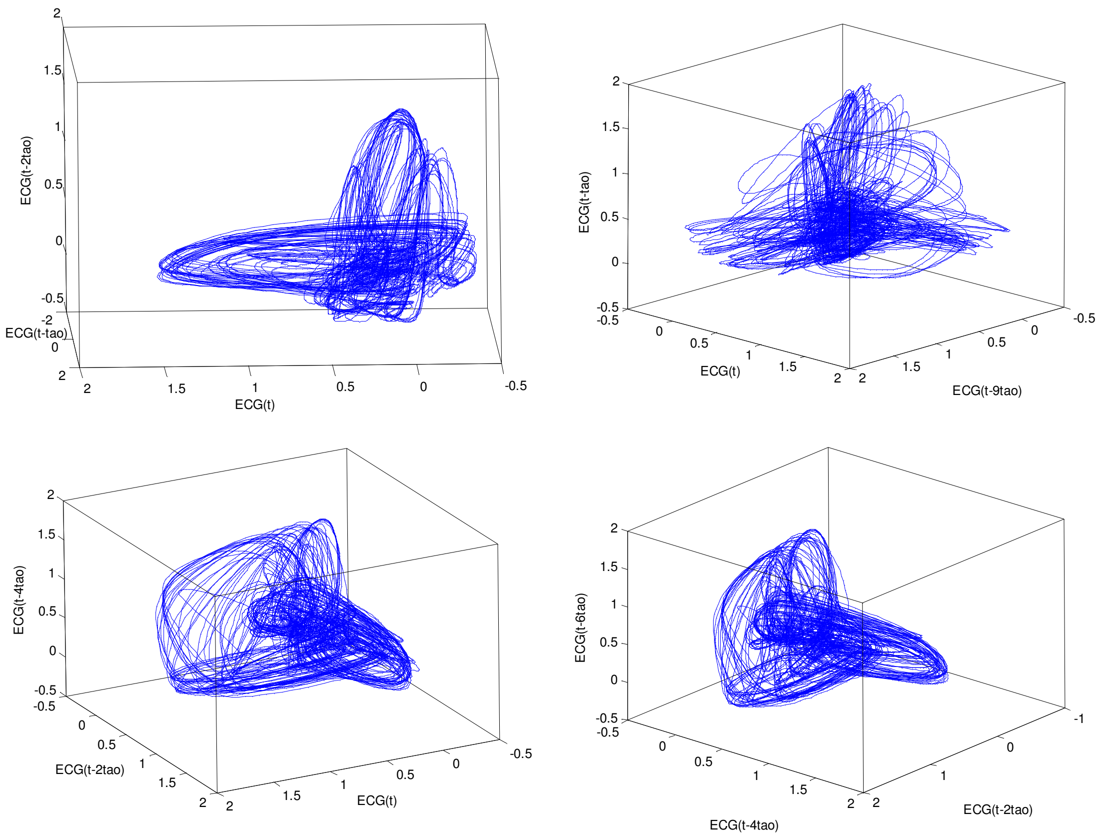

Figure 8. Reconstructed space from ventricular fibrillation ECG.

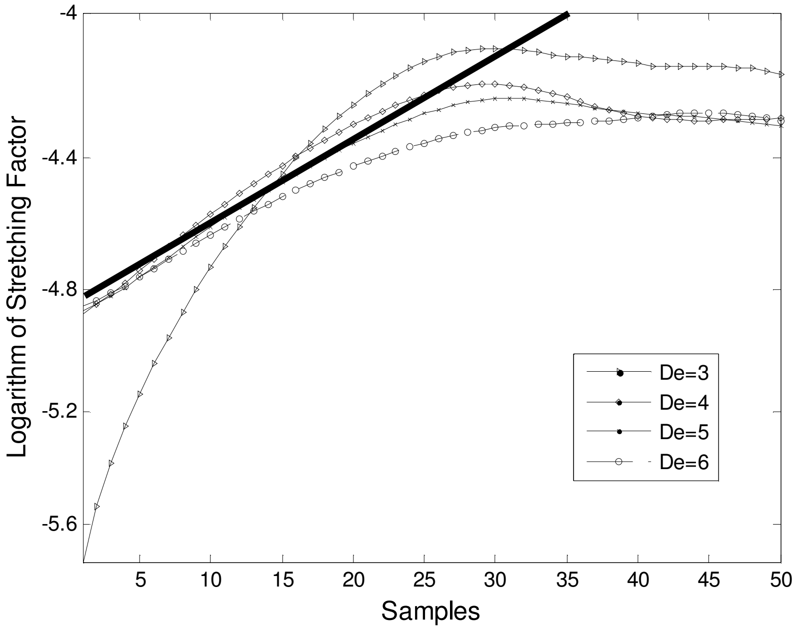

Figure 9. Lyapunov exponents for the ventricular fibrillation ECG.

5. CONCLUSIONS

Time series analysis of the heart rhythms represented by the ECG signal is carried out by considering signals generated from a mathematical model formed by three coupled modified Van der Pol oscillators connected by time delay coupling. Numerical simulations show that the proposed model captures the general behavior of the ECG signals. State space reconstruction and Lyapunov exponents are employed for the analysis. State space reconstruction employs the method of delay coordinates using the method of the average mutual information for the determination of time delay and the method of the false nearest neighbors for the determination of the embedding dimension. Lyapunov exponent estimation employs the Kantz's algorithm. Normal and ventricular fibrillation ECGs are treated. The analysis confirms that normal ECG is related to regular behavior presenting the greatest Lyapunov exponent with null value. On the other hand, ventricular fibrillation ECG signal analysis indicates an increase in time series complexity. The greatest Lyapunov exponent presents a positive value which means that the fibrillation is related to chaos. The developed analysis points that order and chaos are both present in heart rhythms. Therefore, chaos control may be useful to change the heart response. Moreover, it is possible to say that nonlinear dynamics are promising to be applied for clinical purposes.

6. ACKNOWLEDGEMENTS

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