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RANDOMNESS EFFECT ON HEART DYNAMICS ANALYSIS USING MATHEMATICAL MODELS

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Abstract. *A mathematical model composed by three-coupled nonlinear oscillators coupled by time-delayed connections is used to investigate randomness effects on heart rhythm analysis. Accordingly, delayed-differential equations represent heart dynamics. Nondeterministic aspects are contemplated considering random connections among oscillators. The main idea is to show that nonlinearities and randomness define together the great variety of possibilities of heart dynamics. In general, results show that the model is able to capture the main behaviors of the cardiac system and that pathological behavior can evolve from normal rhythms due to random variation.*

Keywords: *Nonlinear dynamics, chaos, cardiac rhythms, DDEs, random*

1. INTRODUCTION

There are different forms to evaluate the heart functioning by measuring some signal. Electrocardiogram (ECG) is one of the most popular measurements that records the heart electrical activity. The electrical impulses related to heart functioning are recorded in the form of waves, which represents the electrical current in different areas of heart.

Heart rate variability (HRV) is one of the best predictors of arrhythmic events (Mansier et al., 1996). HRV may vary considerably even in the absence of physical or mental stress and several measures of HRV have been applied for clinical and research purposes. The existence of HRV points that, besides nonlinear characteristics, heart system can present some random behavior.

Kantz & Schreiber (2002) established a comparison between deterministic chaos and random noise for the heart rhythm analysis. Bozoki (1997) developed a data acquisition method for fetal heart rate suitable to be used by both power spectral analysis (statistical) and chaos theory (deterministic). Kaplan & Cohen (1990) analyzed fibrillatory ECGs of dogs and results suggest that this fibrillation is similar to a random signal. However, an example where deterministic dynamical system can generate random-looking, nonchaotic, behavior was also observed. Yates & Benton (1994) exposed the difficulty to decide between determinist or statistical analysis to deal with human cardiovascular data.

A mathematical model proposed by Cheffer & Savi (2017) is employed to describe heart dynamics. This model considers three oscillators with delayed couplings. Each oscillator is described by a modified Van der Pol oscillator (Van der Pol & Van der Mark, 1928), presented on Grudzinski & Zebrowski (2004). The essential idea is similar to the one discussed on Gois & Savi (2009). This model can reproduce normal ECG and several heart pathologies. The main idea is to show how random couplings can change the ongoing rhythms, inducing different pathologies.

2. MATHEMATICAL MODELING

Heart is a muscular organ activated by electrical stimuli with the function of pumping blood through all the organs and tissues of the body. In mammals, the heart is divided into 4 cavities: 2 atria and 2 ventricles. The heart electrical activity can be understood as a network formed by sinoatrial node (SA), atrioventricular node (AV) and His-Purkinje (HP) complex (Gois & Savi, 2009; Glass, 2009). The initial excitation occurs in the SA node, natural pacemaker, and propagates as a wave, stimulating atria. Upon reaching the AV node, it initiates a pulse that excites the bundle of His, which in turn transmits to the Purkinje fibers. Basically, the electrical impulses generated during cardiac functioning are recorded in the form of waves, which characterize the ECG.

Cardiac system modeling can be made from the coupling of three nonlinear oscillators. Gois & Savi (2009) proposed the use sinoatrial node (SA), atrioventricular node (AV) and His-Purkinje complex (HP) with asymmetrical and bidirectional connections in order to build a general model that is capable of reproducing the cardiac behavior. Figure 1 shows the conceptual model of this approach. In this work, the same idea of the three-coupled oscillators is considered, each one of them described by the model due to Grudzinski & Zebrowski (2004), proposing some modifications.

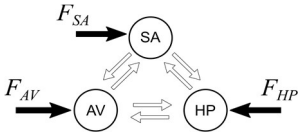

Figure 1 – Conceptual model of the general cardiac functioning.

Therefore, the cardiac system can be modeled by three oscillators (SA, AV and HP) that are coupled by time-delayed terms that represent the transmitting time spent among each one of the oscillators. Under these assumptions, the cardiac system dynamics is governed by the following equations:

$$
\begin{aligned}
\dot{x}_1 &= x_2 \\
\dot{x}_2 &= F_{SA}(t) - \alpha_{SA} x_2 (x_1 - v_{SA_1})(x_1 - v_{SA_2}) - \frac{x_1(x_1 + d_{SA})(x_1 + e_{SA})}{d_{SA} e_{SA}} \\
&\quad - k_{AV-SA} x_1 + k^{\tau}_{AV-SA} x_3^{\tau_{AV-SA}} - k_{HP-SA} x_1 + k^{\tau}_{HP-SA} x_5^{\tau_{HP-SA}} \\
\dot{x}_3 &= x_4 \\
\dot{x}_4 &= F_{AV}(t) - \alpha_{AV} x_4 (x_3 - v_{AV_1})(x_3 - v_{AV_2}) - \frac{x_3(x_3 + d_{AV})(x_3 + e_{AV})}{d_{AV} e_{AV}} \\
&\quad - k_{SA-AV} x_3 + k^{\tau}_{SA-A}\, x_1^{\tau_{SA-AV}} - k_{HP-AV} x_3 + k^{\tau}_{HP-AV} x_5^{\tau_{HP-AV}} \\
\dot{x}_5 &= x_6 \\
\dot{x}_6 &= F_{HP}(t) - \alpha_{HP} x_6 (x_5 - v_{HP_1})(x_5 - v_{HP_2}) - \frac{x_5(x_5 + d_{HP})(x_5 + e_{HP})}{d_{HP} e_{HP}} \\
&\quad - k_{SA-HP} x_5 + k^{\tau}_{SA-HP}\, x_1^{\tau_{SA-HP}} - k_{AV-HP} x_5 + k^{\tau}_{AV-HP}\, x_3^{\tau_{AV-HP}}
\end{aligned}
\tag{1}
$$

By considering indexes *m* and *n* that can represent SA, AV or HP, and $m \neq n$, equation terms are now explained. k_{m-n} and $k^{\tau}{}_{m-n}$ are coupling coefficients between *m* and *n* nodes; and $x_i^{\tau_{m-n}} = x_i(t - \tau_{m-n})$ are delayed terms where τ_{m-n} is the time delay. Since the couplings have temporal lags, the system is governed by delayed differential equations (DDEs). Besides, $F_m(t) = \rho_m \sin(\omega_m t)$ is an external excitation that represents spatiotemporal stimulus and therefore, it is considered as a reduced order representation of spatiotemporal aspects. Note that this external stimulus increases the system dimension based on spatiotemporal information.

The ECG is formed by the signal of each one of the oscillators, being formed by a linear combination of the state variables given by (Gois & Savi, 2009),

$$X = ECG = \beta_0 + \beta_1 x_1 + \beta_2 x_3 + \beta_3 x_5 \tag{2}$$

where β_0, β_1, β_2 and β_3 are constants. Therefore,

$$\dot{X} = \frac{d}{dt}(ECG) = \beta_1 x_2 + \beta_2 x_4 + \beta_3 x_6 \tag{3}$$

Nondeterministic effects are treated considering that oscillator couplings are considered as random variables. Coupling parameters are treated as normal distributions around a mean that represents nominal value, with standard deviations. Based on that, coupling terms can be written as $k_i \sim N\left(\overline{k_i}, \sigma_k^2\right)$ where $\overline{k_i}$ is the mean, nominal value, and σ_k is the standard deviation of the normal distribution.

The fourth order Runge-Kutta method with linear interpolation of time-delayed variables is used to integrate the system (1) (Mensour & Longtin, 1998). In order to treat the DDEs system, it is necessary to approximate their solutions in time instants before τ_j. A Taylor series expansion is proposed (Cunningham, 1954; Gois & Savi, 2009).

$$x_i^{\tau} = x_i - \tau\left(\frac{x_{i+1} - x_i}{h}\right) \tag{4}$$

3. NUMERICAL SIMULATIONS

This work analyses the case where random effects are introduced on SA-AV coupling. It is important to highlight the difference between mean and standard deviation of the coupling distribution ($\overline{k_i}$ and σ_k) and mean and standard deviation on R-R interval histograms μ and σ). The goal is to establish correlations of the standard deviation σ_k with pathologies. Poincaré maps are constructed considering the mean $\mu = 6.403$ (referring to the R-R of the normal rhythm) as the reference period. Consider the SA-AV coupling represented by the parameter $k_{SA-AV} \sim N\left(\overline{k}_{SA-AV}, \sigma_k^2\right)$. Normal heart function has a nominal value $\overline{k}_{SA-AV} = 3$.

Results for different values of standard deviation, σ_k, are presented in Figure 2 showing ECGs. It is noticeable that the increase of σ_k induces a branch block (Canabrava, 2014) changing the ECG characteristic. For σ_k=1.5 response represents incomplete branch block. For values greater than σ_k =2.5, response reaches a complete branch block (absence of QRS complex). Poincaré maps are presented in Figure 3 showing that the increase of σ_k causes the increase of Poincaré map space portion.

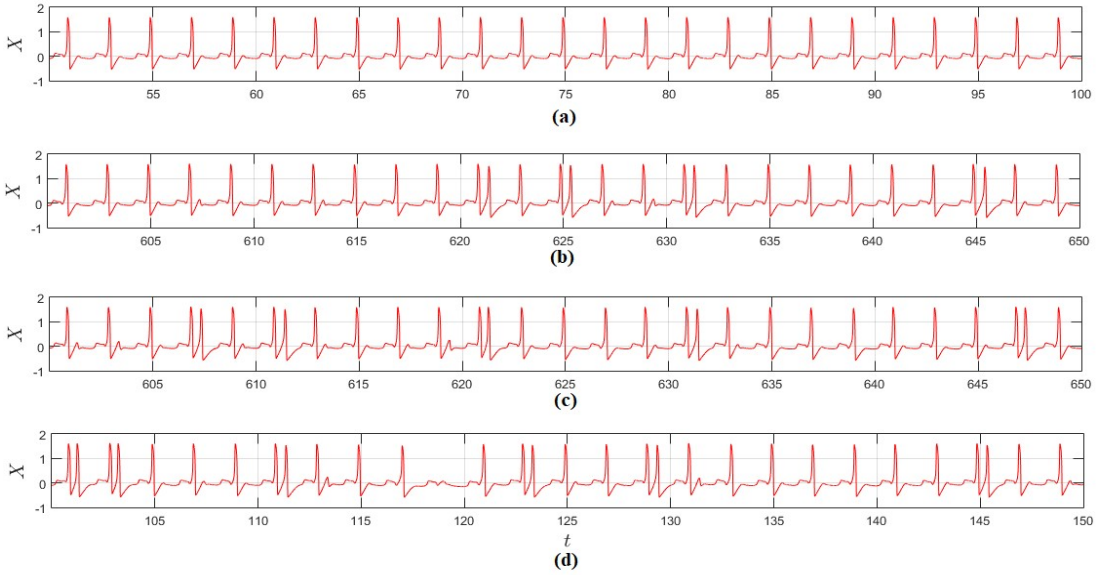

Figure 2 – Random SA-AV coupling ECG.

(a) $\sigma_k = 0.5$; (b) $\sigma_k = 1.5$; (c) $\sigma_k = 2.5$; (d) $\sigma_k = 3.5$.

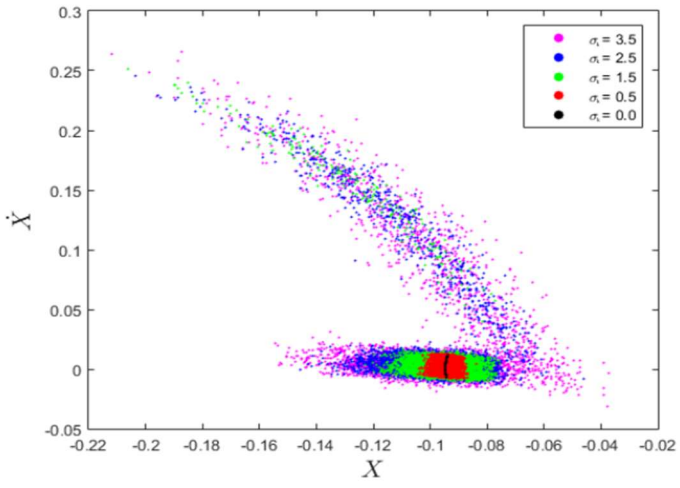

Figure 3 – SA-AV random coupling: Poincaré maps for different standard deviations.

4. CONCLUSIONS

The effects of randomness on the system response are investigated by considering random couplings on mathematical model composed by three-coupled oscillators with time-delayed couplings. The idea is to show that nonlinear and nondeterministic effects can be combined to represent natural system richness. Basically, pathological behaviors can be evolved from normal rhythms due to random couplings. In light of this investigation, it is concluded that cardiac system model has great potential to assist rich heart dynamics comprehension, being useful for disease diagnosis. Nonlinear dynamics analysis, including classical tools as state space and Poincare maps, has proved to be useful for diagnosis because they highlight response variations that are imperceptible on time series.

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