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Bifurcations from normal functioning to pathologies in heart rhythm dynamics using a three-coupled oscillator model

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Abstract: Heart functioning is a rich multiphysics problem involving muscular contractions, electric impulses and blood flows. Heart performs an essential physiological role and, due to that, several mathematical models were developed to describe and reproduce its behavior. Some of these models are related to the electrical impulse of the cardiac rhythm. The muscular contraction is accomplished by the Action Potential (AC), generated in the sinoatrial node, which spreads to the atrioventricular node and later to the His-Purkinje complex. Electrocardiogram (ECG) is a typical cardiac measurement that monitors depolarization and repolarization of the muscular cells. This paper investigates cardiac dynamics employing a model composed by three oscillators coupled by time delayed terms. Numerical simulations are carried out showing normal and pathological functioning, reproducing ECGs. Among pathological behaviors, simulations show atrial flutter, atrial fibrillation, ventricular flutter and atrial fibrillation. Nonlinear tools are employed to analyze system dynamics including Poincaré map, constructed by defining a proper plane in phase space, and Lyapunov exponents that are used to classify each behavior. Bifurcation diagrams are built showing the route from normal functioning to pathological ones.

Keywords: Nonlinear Dynamic, Cardiac Model, Chaotic Response, Fibrillation, Flutter

INTRODUCTION

Different of all other organs the heart is self-excited. The myocardia contraction occur through an electrical activity generated in the Sino-Atrial node (SA). This electrical activity is due to the action potential that propagates as a wave. The first action potential is generated in the cells located in the SA node, which has the role of natural pacemaker, the action potential induces a depolarization wave that is responsible for the myocardia contraction. The depolarization wave diffuses in the atria and part of the wave propagates in the direction of Atrio-Ventricular node (AV). When the wave arrives in the AV node it suffers a process of delay because the atria is not fully depolarized. From the AV the wave goes to a complex called His Purkinje (HP), which let the depolarization wave through the ventricle.

There are two class of cardiac model: one that depicts the cellular function that generated the electrical activity; and another that describes the observed electrical activity in the heart cycle. The first class is closer to the biochemical events. In this context, a very import work in the understanding of action potential creation processes was presented by Hodgkin e Huxley [5] and describes the ionic mechanism implicit in the action potential. After this work, some models were presented in order to describe the biochemical phenomena in the electrical activity. [9, 12]

The second class is close to the physical measurements, where the cardiac cycle can be observed according to the electrical activity generated in the process of myocardia contraction. Van der Pol [10] was the first to investigate this phenomena, where the heart beat is considered as a relaxation oscillation. The model presented by Gois and Savi [3] is based in a Van der Pol modified model presented by Grudziński [4], however three nonlinear oscillator are coupled by a delayed variable, which reproduces electrical activity captured by the Electrocardiogram (ECG).

This paper investigates the nonlinear dynamic of a modified coupled Van der Pol model that reproduce a synthetic ECG. The motion equations consist on six delayed differential equation (DDE) that are numerically integrated using a fourth order Runge Kutta method. For the heart normal functioning no external excitation is considered in the model. Four pathological ECG are reproduced: atrial flutter, atrial fibrilation, ventricular flutter and ventricular fibrillation. At last, bifurcation diagrams are constructed showing the route from normal functioning to ventricular flutter.

CARDIAC MODEL

The model investigated in this work was first presented by Gois and Savi [3], and consists of three coupled modified Van der Pol oscillators. Equations (1) and (2) consists in the first oscillator and represents the sinoatrial node (SN), where the action potential is generated and induces the depolarization wave that is propagated in the direction of the atrioventricular node (AVN). The process of propagating of the depolarization wave from the SN to the AVN is still unclear as presented in the research of [1, 8]. The second oscillator is composed by Eqs. (3) and (3) and represents the AVN, while the third oscillator is represented by Eqs (5) and (6) and is on the concern of the His-Purkinje complex.

$$\dot{x_1} = x_2 \tag{1}$$

$$\dot{x_2} = -\alpha_{SA} x_2 (x_1 - v_{SA1})(x_1 - v_{SA2}) - \frac{x_1 (x_1 + d_{SA})(x_1 + e_{SA})}{d_{SA} e_{SA}} + \rho_{SA} sin(\omega_{SA} t) - x_1 k_{AV-SA} + x_3^{\tau_{AV-SA}} k^*_{AV-SA} - x_1 k_{HP-SA} + x_5^{\tau_{HP-SA}} k^*_{HP-SA} \tag{2}$$

$$\dot{x_3} = x_4 \tag{3}$$

$$\dot{x_4} = -\alpha_{AV} x_4 (x_3 - v_{AV1})(x_3 - v_{AV2}) - \frac{x_3 (x_3 + d_{AV})(x_3 + e_{AV})}{d_{AV} e_{AV}} + \rho_{AV} sin(\omega_{AV} t) - x_3 k_{SA-AV} + x_1^{\tau_{SA-AV}} k^*_{SA-AV} - x_3 k_{HP-AV} + x_5^{\tau_{HP-AV}} k^*_{HP-AV} \tag{4}$$

$$\dot{x_5} = x_6 \tag{5}$$

$$\dot{x_6} = -\alpha_{HP} x_6 (x_5 - v_{HP1})(x_5 - v_{HP2}) - \frac{x_5 (x_5 + d_{HP})(x_5 + e_{HP})}{d_{HP} e_{HP}} + \rho_{HP} sin(\omega_{HP} t) - x_5 k_{SA-HP} + x_1^{\tau_{SA-HP}} k^*_{SA-HP} - x_5 k_{AV-HP} + x_3^{\tau_{AV-HP}} k^*_{AV-HP} \tag{6}$$

where $x_3^{\tau_{AV-SA}} = x_3(t - \tau_{AV-SA})$, $x_5^{\tau_{HP-SA}} = x_5(t - \tau_{HP-SA})$, $x_1^{\tau_{SA-AV}} = x_1(t - \tau_{SA-AV})$, $x_5^{\tau_{HP-AV}} = x_5(t - \tau_{HP-AV})$, $x_1^{\tau_{SA-HP}} = x_1(t - \tau_{SA-HP})$, $x_3^{\tau_{AV-HP}} = x_1(t - \tau_{AV-HP})$, being τ_{AV-HP}, τ_{HP-SA}, τ_{SA-AV}, τ_{HP-AV}, τ_{SA-HP}, τ_{AV-HP} time delays.

When the action potential arrives in the AVN node it suffers a process of delay [6, 11]. The term $x_1^{\tau_{SA-AV}}$ in the Eq. 4 represents this delay. Note that two time delayed terms are introduced in Eqs. 2, 4 and 6 These terms are responsible for coupling the three oscillator.

The combination of the waves generated in the SN, AVN and His-Purkinje complex gives rise to the complete ECG, as presented: $X = ECG = \beta_0 + \beta_1 x_1 + \beta_2 x_3 + \beta_3 x_5$ and $X = \frac{dECG}{dt} = \beta_4 x_2 + \beta_5 x_4 + \beta_6 x_6$ It is considered $\beta_0 = 1mV$, $\beta_1 = 0.06mV$, $\beta_2 = 0.1mV$, $\beta_3 = 0.3mV$, $\beta_4 = 0.06mV$, $\beta_5 = 0.1mV$ and $\beta_6 = 0.3mV$ for all synthetic ECG presented in this work.

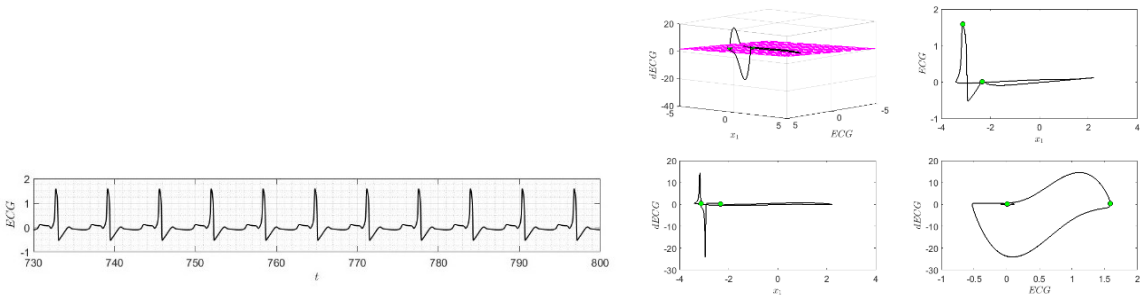
RESULTS

In this section, five cases are analyzed: normal ECG, atrial flutter, atrial fibrillation, ventricular flutter and ventricular fibrillation. These five cases are reproduced numerically using the Delay Differential Equation (DDE) presented in Eqs. [1-6] by using appropriate parameters. The initial conditions used in all simulations are $(x_1(0), x_2(0), x_3(0), x_4(0), x_5(0), x_6(0)) = (-\frac{1}{10}, \frac{1}{40}, -\frac{6}{10}, \frac{1}{10}, -\frac{33}{10}, \frac{10}{15})$. In the numerical integration, while $t < \tau$, the value of the delayed variable are approximated by the Taylor Series [2]. When $t > \tau$, the states already obtained from numerical integration are used as delayed variables. If the state is needed in an intermediate time between two consecutive available points, a linear interpolation is considered.

The following parameters are related to the reproduction of a synthetic ECG obtained by the model, the parameters give a response that correspond to the normal functioning of the heart: $\alpha_{SA} = 3$, $v_{SA1} = 1$, $v_{SA2} = -1.9$, $d_{SA} = 1.9$, $e_{SA} = 0.55$, $\alpha_{AV} = 3$, $v_{AV1} = 0.5$, $v_{AV2} = -0.5$, $d_{AV} = 4$, $e_{AV} = 0.67$, $\alpha_{HP} = 7$, $v_{HP1} = 1.65$, $v_{HP2} = -2$, $d_{HP} = 7$, $e_{HP} = 0.67$, $\rho_{SA} = \rho_{AV} = \rho_{HP} = 0$, $\omega_{SA} = \omega_{AV} = \omega_{HP} = 0$, $k_{SA-AV} = k^*_{SA-AV} = 0$, $k_{AV-HP} = k^*_{AV-HP} = 55$, $k_{SA-HP} = k^*_{SA-HP} = k_{AV-SA} = k^*_{AV-SA} = k_{HP-SA} = k^*_{HP-SA} = k_{HP-AV} = k^*_{HP-AV} = 0$, $\tau_{SA-AV} = 0.8$, $\tau_{AV-HP} = 0.1$, $\tau_{SA-HP} = \tau_{AV-SA} = \tau_{HP-SA} = \tau_{HP-AV} = 0$. The four pathologies presented in this work are obtained by varying the previous parameters, the variation of parameters of each pathology will be presented in the section of each pathology.

Normal Condition

The normal function of the heart is composed by the PQRST wave measured by the Electrocardiogram (ECG). The P wave are related to atria depolarization, the QRS with ventricular depolarization and the T wave represents the ventricular repolarization. Figure 1a presents the response obtained by the model that reproduce a normal ECG, this response has the PQRST complex. The plane in magenta in Fig. 1b is the Poincaré Section, when the trajectory intercept this plane the Poincaré map is formed, presented in green points. The Lyapunov exponents for this condition are $(0.00, -0.20, -0.28, -0.32, -0.33, -0.38)$ that is related to a limit cycle as also mentioned in the work of [7].



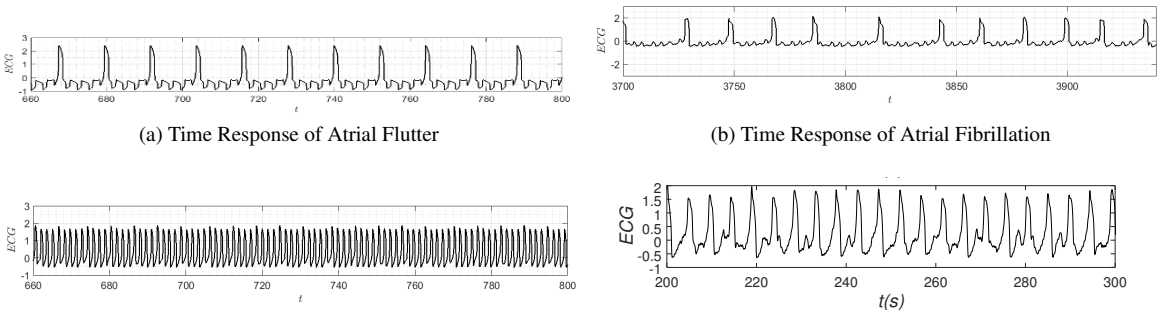
(a) Time Response of the Normal Synthetic ECG

(b) Projection of the Phase Space

Figura 1: Normal Condition

Pathologies

The atrial flutter occurs when the atria starts to beat in a regular abnormal frequency, presenting more than one P wave between two QRS complex. Therefore, it is not possible to identify the R ware in an atrial flutter condition. For the reproduction of this pathology is used the same parameters used in normal condition however some of them receive new value: $v_{SA1} = 1.65$, $v_{SA2} = -4.2$, $\alpha_{AV} = 7$, $k_{SA-AV} = 0.66$, $k^{\tau}_{SA-AV} = 0.02$, $k_{AV-HP} = 14$, $k^{\tau}_{AV-HP} = 60$ and $\tau_{SA-AV} = 0.66$. The Lyapunov Exponents are $(0.00, -0.13, -0.54, -0.87, -0.88, -0.90)$ showing a quasi-periodic behavior.



(a) Time Response of Atrial Flutter

(b) Time Response of Atrial Fibrillation

(c) Time Response of Ventricular Flutter

(d) Time Response of Ventricular Fibrillation

The atrial fibrillation is a condition where the both atrial chambers starts to beat irregular, it is a seriously situation and may be treated as an emergency. In the model it implies that the first oscillator must oscillates in an irregular wave. Same parameters of normal condition are used except for the following that receive new values: $\alpha_{AV} = 7$, $\rho_{SA} = 8$, $\omega_{SA} = 2.1$, $k_{SA-AV} = 0.66$, $k^{\tau}_{SA-AV} = 0.09$, $k_{AV-HP} = 14$, $k^{\tau}_{AV-HP} = 38$. Figure 2b presents the time response, related to the measured ECG in this condition. The Lyapunov exponents are $(0.07, 0.03, -0.21, -0.83, -0.85, -0.88)$ showing that this response is related to hiper chaos condition.

The ventricular Flutter occurs when the ventricle start to beat in a regular abnormal frequency, when it happens it is not possible to identify the wave P and T in the ECG because the complex QRS are hidden this waves. Of the parameters presented in the normal function of the heart only tow should be changed to obtain the Ventricular Flutter: $k_{AV-HP} = 45$ and $k^{\tau}_{AV-HP} = 20$. The Lyapunov Exponets are $(0.00, 0.00, -0.21, -0.83, -0.85, -0.88)$

The ventricular Fibrillation is a condition when the ventricle start to contract non-periodically, this abnormality is a seriously and must be threat with emergency. Assuming the following new parameters: $v_{AV1} = 1.65$, $d_{AV} = 2$, $\alpha_{HP} = 2$, $d_{HP} = 4$, $\rho_{SA} = 8$, $\rho_{AV} = 30$, $\rho_{HP} = 30$, $\omega_{AV} = 2.1$, $\omega_{SA} = 2$, $\omega_{HP} = 15$, $k_{SA-AV} = 1$, $k^{\tau}_{SA-AV} = 1$, $k_{AV-HP} = 3$, $k^{\tau}_{AV-HP} = 0.05$. The ECG presents a characteristic of unpredictable wave as can be seen in the synthetic ECG presented in Fig. 2d . The Lyapunov exponents are $(0.03, 0.00, -0.13, -0.83, -0.84, -0.85)$ showing a chaotic response.

BIFURCATION OF THE NORMAL CONDITION TO VENTRICULAR FLUTTER

The route from normal condition to ventricular flutter is obtained by changing two parameters that are related to the coupling of first and second oscillators: k_{AVHP} and k^{*}_{AVHP}. The variation of parameters is show in the Fig. 2, observe that the normal ECG is in the rightmost side of the graphic. Points in green show the variation of first parameter k_{AVHP}, which is decreased from 55 to 45. In this first step, value of k^{*}_{AVHP} is 55. It can be observed that the system keeps periodic in all range. The second variation is performed for the parameter k^{*}_{AVHP} and is represented by purple points in the diagram. This parameter is decreased from k_{AVHP} of 55 to 20. Observe that the ventricular flutter is reached in the leftmost side of the graphic and a qualitative change in ECG is observed for $k^{*}_{AVHP} = 35$.

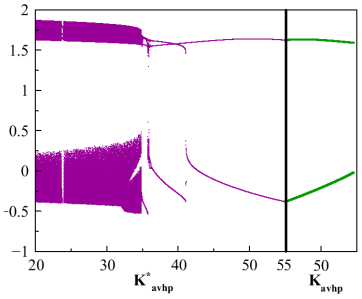


Figura 2

CONCLUSION

This paper address an investigation of the cardiac dynamics from numerical analysis of a three-coupled oscillator model that reproduce a synthetic ECG. The model reproduces the Normal condition and four pathologies. In order to propose a suitable Poincaré Map a proper Section is defined based in a combination of one state variable, ECG and $d(ECG)/dt$. Bifurcation diagrams show the route from normal condition to different pathologies.

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