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HEART RHYTHMS DRIVEN BY CHAOTIC PACEMAKER RESPONSES

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Abstract. *Biological rhythm is an essential characteristic of natural systems that can exhibit regular or irregular dynamical behaviors and can be related to normal or pathological functioning. In this regard, a dynamical analysis can establish relations between responses characteristics and biological functioning. This work performs a dynamical analysis of heart rhythms by using a mathematical model that considers the coupling of three nonlinear oscillators to represent electrical activity, being able to generate electrocardiograms (ECG) of several clinical behaviors. The main idea of the study is investigating natural pacemaker responses and its influence on heart activity, giving special attention to chaotic situations. Nonlinear dynamics tools as bifurcation diagrams, Poincare Maps and Lyapunov exponents are employed. Bifurcation analyses are developed for natural pacemaker and chaotic responses, selecting some drives to the cardiac system model. A great variety of ECG behaviors is treated, revealing to be relevant cardiac arrhythmias as branch blocks and junctional tachycardia that may lead to dangerous rhythms, and P and T wave alternations.*

Keywords: *Nonlinear dynamics, chaos, cardiac rhythms, DDEs, Poincare maps*

1. INTRODUCTION

Several studies suggest that chaotic dynamics is desirable for biological systems in order to increase their adaptability (Pool,1989; Goldberger *et al.*, 1990; Skinner *et al.*,1990). According to Pool (1989): "chaos may provide a healthy flexibility to the heart, brain, and other parts of the body". Classical dynamical invariants are widely applied to characterize biochaos, including power spectrum, fractal dimension and short-term predictability, having the Lyapunov exponents as the most widespread method. Chaos identification in cardiac and neural systems has attracted a lot of attention of scientific community, being possible to be performed by using time series analysis (Herbschleb *et al.*, 1980; Chen *et al.*, 1998; Skanes *et al.*, 1998; Glass and Mackey,1988; Rapp, 1993). A commonly used time series for heart dynamics capturing is the Electrocardiogram (ECG), that records the heart electrical activity in waveforms.

Heart dynamics can be alternatively analyzed by mathematical model perspective. The first mathematical model to describe heart dynamics was proposed by Van der Pol and Van der Mark (1928). Grudzinski and Zebrowski (2004) proposed a more accurate natural pacemaker mathematical model by including alterations on the original Van der Pol (VdP) oscillator. In order to describe cardiac system, several studies developed models by coupling modified VdP oscillators. Gois and Savi (2009) proposed bidirectional and time delayed coupling of three oscillators that represent sinoatrial (SA) and atrioventricular (AV) nodes and His-Purkinje (HP) complex functioning. Cheffer *et al.* (2021) improved the three-coupled oscillator model due to Gois and Savi (2009) by including alternations in coupling terms. A qualitative comparison between experimental and model-generated ECG signals showed that the model is able to reproduce several biorhythms. Nonlinear tools were also applied to help rhythm characterization and bifurcation analysis were presented showing possible routes from normal to pathological responses.

This work deals with biochaos in cardiac systems considering that the electrical activity of the heart is modeled by three coupled oscillators. Based on that, synthetic ECG can be represented describing the cardiac system behavior. The strategy is to investigate the influence of different kinds of behaviors of the natural pacemaker, the sinoatrial node, on the ECG responses. A global comprehension of the natural pacemaker behavior is provided by the analysis of bifurcation diagrams that are built varying dissipation and external stimulus of the SA oscillator. This analysis allows one to identify dif- ferent kinds of behaviors including chaotic responses. The influence of these kinds of behaviors on the electrical activity of the heart, represented by ECGs, is investigated establishing a connection with distinct pathologies. Special attention is dedicated to the effect of chaotic driven signals.

2. MATHEMATICAL MODELING

The model proposed by Grudzinski and Zebrowski (2004) is a modification of the original Van der Pol oscillator replacing the restitution force by a cubic function being expressed as follows:

$$\ddot{x} + \alpha\dot{x}(x - \nu_1)(x - \nu_2) + \frac{x(x+d)(x+e)}{d\,e} = F(t), \tag{1}$$

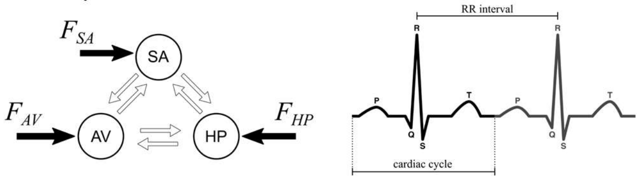
where α defines the pulse shape, characterizing the time when the heart receives the stimulus; ν_1 and ν_2 determine the signal amplitude, and to preserve the self-excitatory nature, $\nu_1\nu_2 < 0$; and $F(t)$ is an external stimulus.

The cardiac system is modeled from the coupling of three nonlinear oscillators representing SA node, AV node and HP complex (Figure 1a). Asymmetrical and bidirectional connections are employed in order to build a general model that is capable to reproducing the electrical activity of the heart including normal and pathological functioning. Under these assumptions, the system is governed by the following equations (Cheffer *et al.*, 2021):

$$\begin{aligned}
\dot{x}_1 &= x_2 \\
\dot{x}_2 &= F_{SA}(t) - \alpha_{SA}x_2(x_1 - \nu_{SA_1})(x_1 - \nu_{SA_2}) - \frac{x_1(x_1 + d_{SA})(x_1 + e_{SA})}{d_{SA}e_{SA}} - k_{AV-SA}x_1 + k^{\tau}_{AV-SA}x_3^{\tau_{AV-SA}} \\
&\quad - k_{HP-SA}x_1 + k^{\tau}_{HP-}\;\; x_5^{\tau_{HP-SA}} \\
\dot{x}_3 &= x_4 \\
\dot{x}_4 &= F_{AV}(t) - \alpha_{AV}x_4(x_3 - \nu_{AV_1})(x_3 - \nu_{AV_2}) - \frac{x_3(x_3 + d_{AV})(x_3 + e_{AV})}{d_{AV}e_{AV}} - k_{SA-AV}x_3 + k^{\tau}_{SA-AV}x_1^{\tau_{SA-A}} \\
&\quad - k_{HP-AV}x_3 + k^{\tau}_{HP-AV}x_5^{\tau_{HP-AV}} \\
\dot{x}_5 &= x_6 \\
\dot{x}_6 &= F_{HP}(t) - \alpha_{HP}x_6(x_5 - \nu_{HP_1})(x_5 - \nu_{HP_2}) - \frac{x_5(x_5 + d_{HP})(x_5 + e_{HP})}{d_{HP}e_{HP}} - k_{SA-HP}x_5 + k^{\tau}_{SA-HP}\,x_1^{\tau_{SA-HP}} \\
&\quad - k_{AV-HP}x_5 + k^{\tau}_{AV-HP}\,x_3^{\tau_{AV-H}}
\end{aligned} \tag{2}$$

The indexes *m* and *n* represent SA, AV or HP, being $m \neq n$. Equation terms are now explained: k_{m-n} and k^{τ}_{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. Thus, the system is governed by delayed differential equations (DDEs). Besides, $F_m(t) = \rho_m\, sin(\omega_m\, t)$ is an external excitation that has origin in spatiotemporal stimulus and therefore, it is considered as a reduced order representation of spatiotemporal aspects (Skanes *et al.*, 1998; Jalife *et al.*, 1998).

In Figure 1b, a schematic picture of a normal cardiac cycle, highlight the main waves: P wave representing SA node impulse; QRS complex that is formed by ventricular contraction; and T wave that reflects ventricular repolarization.



(a) (b)

Figure 1. Conceptual model of the general cardiac functioning (a). Scheme of normal cardiac cycle (b).

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),

$$X = ECG = \beta_0 + \beta_1 x_1 + \beta_2 x_3 + \beta_3 x_5\,, \tag{3}$$

where $\beta_0 = 1\,mV$, $\beta_1 = 0.06\,mV$, $\beta_2 = 0.1\,mV$ and $\beta_3 = 0.3\,mV$.

3. NUMERICAL SIMULATIONS

The solution of system (1) is numerically obtained by using the fourth order Runge-Kutta method with linear interpolation of time-delayed variables to approximate their solutions in time instants before τ_j (Mensour and Longtin, 1998). For the interpolation, a Taylor series expansion is proposed (Cunningham, 1954; Gois & Savi, 2009):

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

Table 1 contains parameters used in all simulations, vanishing all other parameters that are not presented. They refer to normal rhythm which has unidirectional couplings in such a way that the electrical impulse is conducted from SA to AV node and then, from AV node to HP complex. This means that the system does not present external stimuli. A convergence analysis reveals that time steps smaller than 10^{-3} presents error of the order of 10^{-6}, considered satisfactory.

Table 1. Cardiac system parameters for normal rhythm (Cheffer *et al.*, 2021).

SA oscillator		**AV oscillator**		**HP oscillator**		**Couplings**		**Time delays**		**Initial conditions**	
α_{SA}	3	α_{AV}	3	α_{HP}	7	k_{SA-AV}	3	τ_{SA-AV}	0.8	$x_1(0)$	-0.1
ν_{SA_1}	1	ν_{AV_1}	0.5	ν_{HP_1}	1.65	k_{AV-HP}	55	τ_{AV-HP}	0.1	$x_2(0)$	0.025
ν_{SA_2}	-1.9	ν_{AV_2}	-0.5	ν_{HP_2}	-2	k^{τ}_{SA-AV}	3			$x_3(0)$	-0.6
d_{SA}	1.9	d_{AV}	4	d_{HP}	7	k^{τ}_{AV-HP}	55			$x_4(0)$	0.1
e_{SA}	0.55	e_{AV}	0.67	e_{HP}	0.67					$x_5(0)$	-3.3
										$x_6(0)$	2/3

3.1 Natural Pacemaker

A bifurcation diagram for pacemaker model (Eq. 1) was built by using Poincare maps based on return map considering a secant section. Poincare section is built considering a section orthogonal to $\{x_1, x_2\}$ in $x_2 = 0$ and transversal intersections in negative x_2 direction are collected. Initial conditions (Table 1) are $\{x_1, x_2\} = \{-0.1, -0.025\}$. It was evaluated the influence of amplitude ρ of external stimulus, $F(t) = \rho\, sin(\omega\, t)$.The considers $\rho \in [0, 10]$ with steps of 0.025 and simulations with $t \in [0, 5000]$. Frequency is constant, $\omega = 2.1$, representing relation between normal rhythm and AF frequencies (Cheffer *et al.*, 2021). The other parameters refer to SA oscillator in Table 1.

Figure 2 presents bifurcation diagram, identifying four responses with chaotic-like behaviors. Each response has one positive Lyapunov exponent (estimated with algorithm due to Wolf *et al.*, 1985), which assure the existence of chaos. The following values are obtained for the maximum exponents: Response 1 - 0.06; Response 2 - 0.10; Response 3 - 0.14; Response 4 - 0.13.

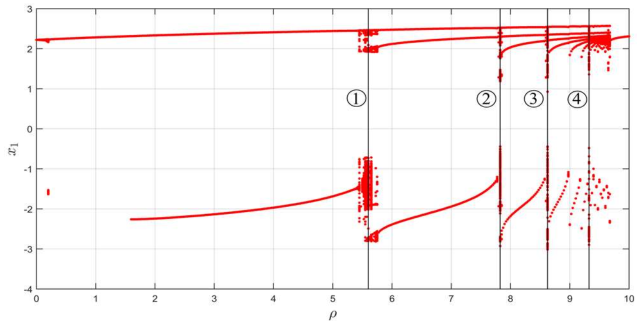


Figure 2. Pacemaker model bifurcation diagram for external stimulus amplitude ρ, highlighting four chaotic responses.

3.2 Cardiac system

The chaotic natural pacemaker behaviors identified in the preceding section are employed in order to evaluate the resulting cardiac system (Eq. 2) behavior represented by the ECG shown in Figure 3. Note that ECG presents non-periodic rhythms, with irregular occurrence of R peaks, which is a characteristic of atrial tachycardia. In addition, double R peaks are identified that is associated with branch blocks. Alternations of the P and T waves are observed as well. P wave deviations are related to junctional tachycardia (Brugada *et al.*, 1991). Historically, the development of proper methods for identification of alternation of T waves is of great interest, since T wave alternations are useful as clinical indicator of cardiac sudden death (Barbosa *et al.*, 2004). State spaces are characterized by filled regions around large loops.

4. CONCLUSIONS

Heart dynamics was treated by a mathematical model perspective represented by the coupling of three nonlinear oscillators that represent the main heart nodes: SA, AV and HP complex. Cardiac rhythms are investigated from different rhythms of the natural pacemaker - SA node. By using a bifurcation diagram, it was possible to identify chaotic behaviors of pacemaker and confirmed by Lyapunov exponents calculation. The effect of these rhythms in the electrical activity of the cardiac system, represented by ECGs, is then analyzed. A great variety of ECG behaviors is investigated pointing to relevant cardiac arrhythmias as branch blocks and junctional tachycardia that may lead to dangerous rhythms as atrial and ventricular fibrillations.

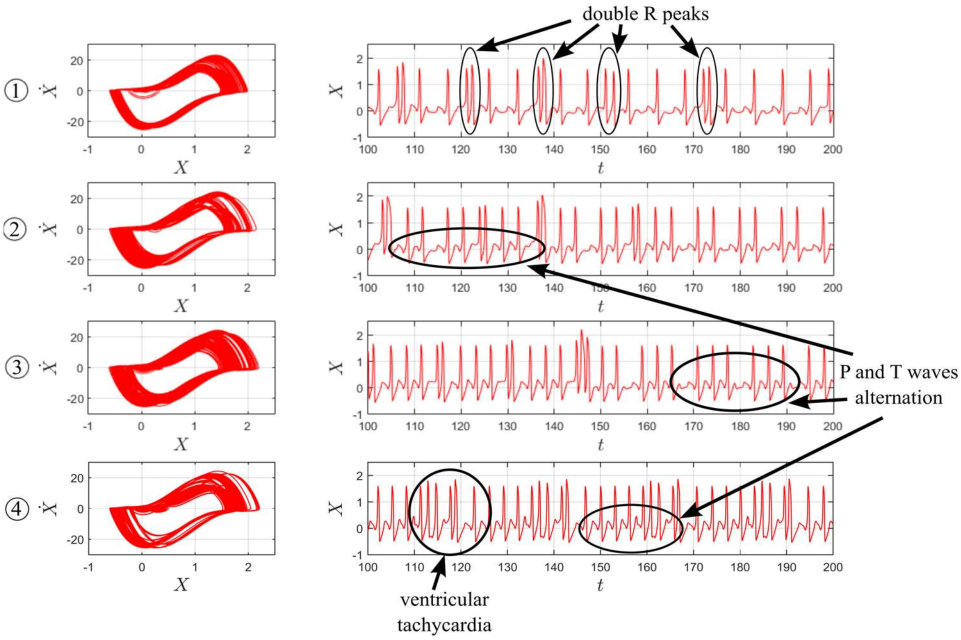


Figure 3. Simulated ECGs driven by selected responses in bifurcation diagram: (left) state spaces, (right) time series. Pathological characteristics are highlighted.

5. ACKNOWLEDGEMENTS

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6. REFERENCES

Barbosa, P.R.B., Barbosa Filho, J., Bonfim, A.D.S., Barbosa, E.C., Boghossian, S.H.C., Ribeiro, R.L., Ginefra, P., 2004. "Alternância Elétrica da Onda T: bases eletrofisiológicas e aplicações clínicas baseadas em evidências". *Revista da SOCERJ*, Vol. 17, pp. 227-242.

Brugada, P., Brugada, J., Mont, L., 1991. "A new approach to the differential diagnosis of a regular tachycardia with a wide QRS complex". *Circulation*, Vol. 83, No. 5, pp. 1649-1659.

Cheffer, A., Savi, M.A., Pereira, T.L., de Paula, A.S, 2021b. "Heart rhythm analysis using a nonlinear dynamics perspective". *Applied Mathematical Modelling*, Vol. 96, pp. 152-176.

Chen, P S., Garfinkel, A., Weiss, J.N., Karagueuzian, H.S., 1998. "Computerized mapping of fibrillation in normal ventricular myocardium". *Chaos*, v. 8, n. 1, p. 127-136.

Cunningham, W.J., 1954. "A nonlinear differential-difference equation of growth", *Proceedings of the National Academy of Sciences*, Vol. 40, No. 8, pp. 708-713.

Glass, L., Mackey, M.C., From Clocks to Chaos: The Rhythms of Life (Princeton University Press, Princeton, 1988).

Gois, S.R.S.M., Savi, M.A., 2009. "An analysis of heart rhythm dynamics using a three-coupled oscillator model". *Chaos, Solitons & Fractals*, Vol. 41, No. 5, pp. 2553-2565.

Goldberger, A.L., Rigney, D.R., and West, B.J., 1990. "Chaos and fractals in human physiology". *Scientific American*, Vol. 262, No. 2, p. 42-49.

Grudzinski, K., Zebrowski, J. J., 2004. "Modeling Cardiac Pacemakers with Relaxation Oscillators". *Physica A*, Vol. 336, pp. 153-162.

Herbschleb, J.N., Heethaar, R.M., Tweel, I., Meijler, F.L., 1980. "Frequency analysis of the ECG before and during ventricular fibrillation". *Computers in Cardiology*, pp. 365-368.

Jalife, J., Berenfeld, O., Skanes, A., Mandapati, R., 1998. "Mechanisms of atrial fibrillation: mother rotors or multiple daughter wavelets, or both?". *Journal of cardiovascular electrophysiology*, Vol. 9, No. 8 Suppl, p. S2.

Mensour, B., Longtin, A., 1998. "Power spectra and dynamical invariants for delay-differential and difference equations". *Physica D: Nonlinear Phenomena*, Vol. 113, No. 1, pp. 1-25.

Pool, R., 1989. "Is it healthy to be chaotic?". Science, Vol. 243, pp. 604–607.

Rapp, P.E., 1993. "Chaos in the neurosciences: Cautionary tales from the frontier," *Biologist (London)*, Vol. 40, pp. 89–94.

Skanes, A.C., Mandapati, R., Berenfeld, O., Davidenko, J.M., Jalife, J., 1998. "Spatiotemporal periodicity during atrial fibrillation in the isolated sheep heart". *Circulation*, Vol. 98, No. 12, pp.1236-1248.

Skinner, J.E., Goldberger, A.L., Mayer-Kress, G., Ideker, R.E., 1990. "Chaos in the heart: Implications for clinical cardiology". *Nature Biotechnology*, Vol. 8, pp.1018–1024.

Van Der Pol, B., Van Der Mark, J., 1928. "The Heartbeat Considered as a Relaxation Oscillator and an Electrical Model of the Heart". *Philosophical Magazine*, Vol.6, pp.763-775.

Wolf, A., Swift, J.B., Swinney, H.L., Vastano, J.A., 1985. "Determining Lyapunov exponents from a time series". *Physica D: Nonlinear Phenomena*, Vol. 16, No. 3, pp. 285-317.

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