E3S Web of Conferences **401**, 05091 (2023) https://doi.org/10.1051/e3sconf/202340105091
CONMECHYDRO - 2023

Stability of equilibrium points of equation of regulatory mechanisms of cardiac activity

M. B. Hidirova[1*], and *Z. Dj.* Yusupova[2, 3]

[1]Research Institute for Development of Digital Technologies and Artificial Intelligence, Tashkent, Uzbekistan
[2]Fiscal Institute Under the State Tax Committee of the Republic of Uzbekistan, Tashkent, Uzbekistan,
[3]"Tashkent Institute of Irrigation and Agricultural Mechanization Engineers" National Research University, Tashkent, Uzbekistan

Abstract. The article presents a mathematical model of regulatory mechanisms of cardiac activity in the form of system of functional-differential equations with delay arguments. With the use of reduction and scaling methods, the system of equations is reduced to the form of a functional-differential equation with delay argument. The equation was qualitatively analyzed. Equilibrium points are revealed and their stability is analyzed. As a result of a qualitative analysis, it was revealed that the mathematical model can reflect various modes of regulatory mechanisms of cardiac activity in normal conditions and in case of anomalies, the modes such as stationary, auto-oscillating, dynamic chaos, "black hole" and falling state.

1 Introduction

Today in the modern world, all areas of our activity, technique, technology, medicine, science and education, the sphere of economics, etc. are rapidly developing and improving. At the same time, a lot of research is also being carried out in medicine, new opportunities are opening up and modern methods of treatment are being developed. However, nowadays the number and types of diseases are gradually increasing. Doctors and researchers are actively continuing to research prevention methods and develop methods of treatment these modern diseases. But, if we look at the statistics of the causes of death of humanity from different cases, among them the first place is taken by heart diseases. This means that cardiologists must thoroughly research and find new opportunities to improve existing methods of preventing and treating heart disease. In this direction, it is possible to obtain better results by applying modern information and communication technologies in the study of cardiac activity and its regulatory mechanisms. By studying the regulatory mechanisms of the heart, it is possible to study the causes of cardiac dysfunctions and diseases. A number of scientific studies to study cardiac activity can be seen today. Scientific work [1] considered the problem of studying the physiology of the heart through mathematical modeling of the process of excitation-contraction of heart muscle fibers. In research [2] were created the model and computer simulation to study the dynamics of the adaptive

*Corresponding author: zaynabhon@inbox.ru

processes that manifest in a healthy cardiovascular system under the certain state of the body. The developed computer simulation can be used to continuous observation of the dynamics of the parameters of the cardiovascular system and the body, which cannot be measured in a direct experiment. As well as, in [3-5] studies cardiac activity is mathematically modeled at the cellular level, cardiomyocytes are considered as an excitable biological system and the mechanisms of cardiac activity are studied by means of mathematical modeling and computer simulation of the excitation of cardiomyocytes, various processes occurring in cardiomyocytes and cardiac contraction.

This work also provides a study of the regulatory mechanisms of cardiac activity by means of mathematical modeling of the process of propagation of excitation waves along the cardiac conduction system.

Mathematical model of regulatory mechanisms of cardiac activity. It is known that the heart is an organ that provides the human body with the necessary oxygen and nutrients through the circulatory system. If we look at the structure of the heart, it has right and left atriums and ventricles. In each cycle of the heart, as a result of the contraction of the muscles in these parts, the next portion of blood is delivered to the arterial vessel under a certain pressure. Such activity of the heart is controlled by an excitation wave generated at the SA node in the upper part of the left ventricle and propagating to the heart components throughout the cardiac conduction system. The excitation wave from the SA node is transmitted to the atriums and the AV node, and then to the right and left ventricles via the bundle of His. It is possible to study the regulatory mechanisms of cardiac activity by mathematically modeling the excitation wave propagation throughout the cardiac conduction system and the excitation process of cardiac parts and nodes. We will consider the problem of mathematical modeling by expressing the propagation of the excitation wave between these sections by the following system of equations.

In the mathematical representation of the process of wave propagation through the cardiac conducting system, it is necessary to take into account the spatio-temporal relationships. This leads to the use of functional-differential equations with delay [6-10]. More general laws of regulatory mechanisms of cardiac activity can be studied using the following system of equations in a simpler form [11]:

$$
\begin{array}{l}
\text{SA:}\\
\text{RA:}\\
\text{LA:}\\
\text{AV:}\\
\text{RV:}\\
\text{LV:}
\end{array}
\begin{cases}
\dfrac{dx(t)}{dt} = \dfrac{a_1\Theta(t-h)\eta(t-h)}{(1+\sigma_1{}^2\Theta^2(t-h))(1+\sigma_2{}^2\eta^2(t-h))} - b_1x(t),\\
\dfrac{dy(t)}{dt} = a_2x(t-h) - b_2y(t),\\
\dfrac{dz(t)}{dt} = a_3x(t-h) - b_3z(t),\\
\dfrac{dv(t)}{dt} = \dfrac{a_4x(t-h)y(t-h)z(t-h)}{1+\sigma_3{}^2x^2(t-h)y^2(t-h)z^2(t-h)} - b_4v(t),\\
\dfrac{d\Theta(t)}{dt} = a_5v(t-h) - b_5\Theta(t),\\
\dfrac{d\eta(t)}{dt} = a_6v(t-h) - b_6\eta(t),
\end{cases}
\tag{1}
$$

$$
\begin{array}{l}
x(t)=\varphi(t),\ y(t)=\varphi(t),\ z(t)=\varphi(t),\ v(t)=\varphi(t),\\
\Theta(t)=\varphi(t),\ \eta(t)=\varphi(t),\ t\in[0,h],
\end{array}
$$

where $a_i,\ b_i,\ i=1,2,\dots,6$ - parameters representing the rates of increase and decrease of activity of excitation in the nodes and heart parts, i.e SA node, right and left ventricles, AV node, right and left ventricles , respectively; $\sigma_i,\ i=1,2,3$ - excitation inhibition coefficients at SA and AV nodes; h - the delay time in the propagation of the excitation wave between the parts of the heart.

The system of functional-differential equations with delays (1) represents the activity of the regulatory mechanisms of the process of propagation of the excitation wave in the heart. Determining the exact solutions of (1), the basic modes and properties derived from them is very complicated due to the nonlinearity of the considered equations and the large number of parameters and variables in it. In this case, the qualitative analysis of (1), the development and implementation of a method for obtaining numerical solutions on a computer is a complex issue. Therefore, (1) can be simplified by using the reduction method and scaling operations [11] and lead the following form.

$$\frac{1}{h}\frac{dZ(\theta)}{d\theta}=\frac{AZ^6(\theta-1)(1+BZ^6(\theta-1))^2}{((1+BZ^6(\theta-1))^2+CZ^6(\theta-1))((1+BZ^6(\theta-1))^2+DZ^6(\theta-1))}- \\ -b_1Z(\theta), \qquad (2)$$

$$\theta>1,\ Z(\theta)=\varphi(\theta),\ \ \theta\in[0,1],$$

where $Z(\theta)$ - activity of cardiac conduction system; A, B, C, D, b_1 - nonnegative parameters.

All parameters of (2) have a non-negative value. Because only in this case, the solutions of the equation representing the activity of cardiac conduction system can make biological sense.

It is known that in the norm, cardiac activity consists of periodic oscillations and, in anomalous cases, non-periodic oscillations. We qualitatively analyze whether the solutions of (2) can represent the oscillating state in cardiac activity. It examines the existence, continuity, non-negativity, limitation and uniqueness of the solutions of (2), the existence of equilibrium points and their stability properties. A qualitative analysis of the properties of solutions to (2) is given in the work [12].

The presence of equilibrium points.

Let's determine the equilibrium points of (2). To do this, we assume that the state of the system does not change over time in the equilibrium state, that is, we define (2) as $\frac{dZ(\theta)}{d\theta}=0$ in the equilibrium state. In this case, it is appropriate to denote $Z(\theta)=Z(\theta-1)=z_0$, and (2) can be written as:

$$\frac{Az_0{}^6(1+Bz_0{}^6)^2}{((1+Bz_0{}^6)^2+Cz_0{}^6)((1+Bz_0{}^6)^2+Dz_0{}^6)}=b_1z_0, \qquad (3)$$

Using (3), we find the equilibrium points. It can be seen that there always exists a trivial equilibrium point $z_0=0$. Since (3) is a complex and nonlinear, it is impossible to determine its solutions. Therefore, to determine the number of non trivial solutions, we draw graphs by defining the right and left sides of (3) with separate functions.

$$F_1=\frac{Az_0^6(1+Bz_0^6)^2}{((1+Bz_0^6)^2+Cz_0^6)((1+Bz_0^6)^2+Dz_0^6)}, \\ F_2=b_1z_0. \qquad (4)$$

It became known that in case of $z_0 = 0$ it will be $F_1 = 0$ and in case of $z_0 \to \infty$ it will be $F_1 \to 0$. To draw a graph of a function F_1, we determine the number of its extremums. It was found that the function F_1 reaches an extremum value at point $z_{0_2} = \frac{1}{\sqrt[6]{B}}$. If the condition

$$B\frac{\sqrt{D}-\sqrt{C}}{\sqrt{C}D-C\sqrt{D}} < \frac{1}{4} \tag{5}$$

is satisfied, it follows that the function F_1 has the third and fourth extremums in the following form:

$$z_{0_{3,4}} = \sqrt{\frac{1 \pm \sqrt{1-4B\sqrt{\frac{\sqrt{D}-\sqrt{C}}{\sqrt{C}D-\sqrt{D}C}}}}{2B\sqrt{\frac{\sqrt{D}-\sqrt{C}}{\sqrt{C}D-\sqrt{D}C}}}},$$

Therefore, the graph of the function F_1 can have three extremums. This leads to the presence of 4 positive equilibrium points $\alpha, \beta, \gamma, \mu (O < \alpha < \beta < \gamma < \mu)$ (Fig. 1).

Normally, in cardiac activity, only the SA node acts as a pacemaker, and in the case of dysfunction of this node (partial or complete blockade), the AV node, i.e., the second-order pacemaker, acts as a heart rhythm controller. The fact that the AV node acts as a pacemaker indicates an arrhythmia condition. The appearance of three extreme points on the graph of equation F_1 corresponds to such a situation (Fig. 2). Since only the appearance of a single extreme in the graph corresponds to the normal functioning of the heart, we consider the case where (2) has two positive equilibrium points in addition to the trivial equilibrium point, i.e., the case where condition (5) is not satisfied.

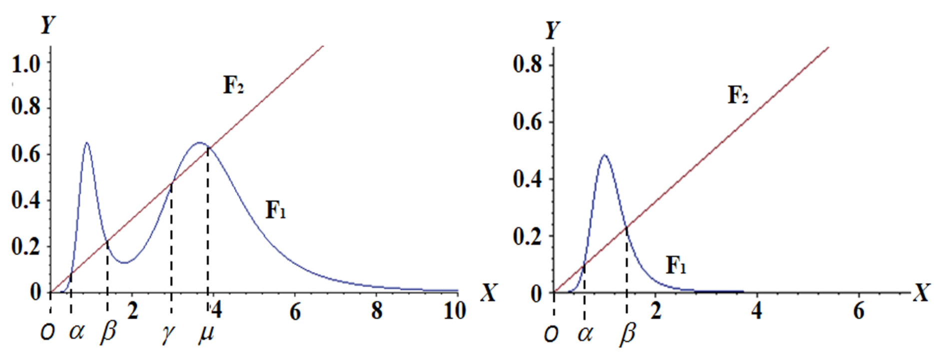

Fig. 1. Presence of equilibrium points

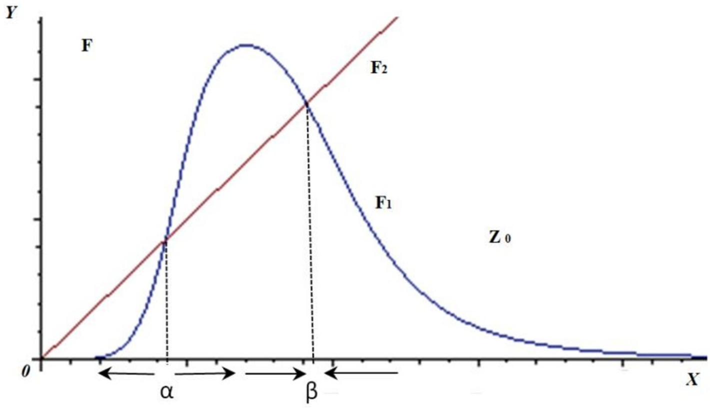

Fig. 2. Properties of equilibrium points in (1)

Consider the cases where (2) has positive non trivial equilibrium points. To check the stability of the equilibrium point z_0, we construct a linear equation that is very close to the equilibrium point. To do this, we add $z(\theta)$, which is very small in value to z_0 [1].

$$Z(\theta) = z_{.} + z(\theta),\ Z(\theta-1) = z_{.} + z(\theta-1)$$

In this case, (1) can be written as follows:

$$\frac{1}{h}\frac{d(z_0+z(\theta))}{d\theta} =$$

$$= \frac{A(z_0+z(\theta-1))^6(1+B(z_0+z(\theta-1))^6)^2}{((1+B(z_0+z(\theta-1))^6)^2+C(z_0+z(\theta-1))^6)((1+B(z_0+z(\theta-1))^6)^2+D(z_0+z(\theta-1))^6)} -$$

$$-b_1(z_0+z(\theta)).$$

In the above expression, since the values of $z(\theta)$ and $z(\theta-1)$ are very small, their squares and higher levels, as well as the terms which include their multiplications, can be ignored, since their values are very close to 0. After doing some mathematical calculations and substitutions, we get the following form:

$$\frac{1}{h}\frac{dz(\theta)}{d\theta} =$$

$$6b_1\left[\frac{1+3Bz_0^{\,6}}{1+Bz_0^{\,6}} - \frac{z_0^{\,6}(D+2B(1+Bz_0^{\,6}))}{(1+Bz_0^{\,6})^2+Dz_0^{\,6}} - \frac{z_0^{\,6}(C+2B(1+Bz_0^{\,6}))}{(1+Bz_0^{\,6})^2+Cz_0^{\,6}}\right]z(\theta-1) - \tag{6}$$

$$-b_1 z(\theta).$$

Equation (6) is a linearized equation around the equilibrium point of (2).

Stability of equilibrium points. To study the properties of solutions of (6), the Hayes criteria can be used [6-8]. To do this, we construct the characteristic equation of (6). We enter the following notations:

 https://doi.org/10.1051/e3sconf/202340105091

$$z(\theta)=e^{\lambda\theta};\ \frac{dz(\theta)}{d\theta}=\lambda e^{\lambda\theta};\ z(\theta-1)=e^{\lambda(\theta-1)}=\frac{e^{\lambda\theta}}{e^{\lambda}}; \tag{7}$$

Substituting the introduced notation (7) into (6), we obtain the following equation:

$$(\lambda+b_1h)e^{\lambda}+6b_1h\left[\frac{z_0{}^6(D+2B(1+Bz_0{}^6))}{(1+Bz_0{}^6)^2+Dz_0{}^6}+\frac{z_0{}^6(C+2B(1+Bz_0{}^6))}{(1+Bz_0{}^6)^2+Cz_0{}^6}-\frac{1+3Bz_0{}^6}{1+Bz_0{}^6}\right]=0, \tag{8}$$

(8) is a characteristic equation of (6) linearized around the equilibrium point. We examine the properties of the solutions of this characteristic equation (8) according to the three conditions of the Hayes criterion and obtain the following generalized condition (9). Every equilibrium point that satisfies this inequality is stable.

$$-\frac{1}{6}<\frac{z_0{}^6(D+2B(1+Bz_0{}^6))}{(1+Bz_0{}^6)^2+Dz_0{}^6}+\frac{z_0{}^6(C+2B(1+Bz_0{}^6))}{(1+Bz_0{}^6)^2+Cz_0{}^6}-\frac{1+3Bz_0{}^6}{1+Bz_0{}^6}<\frac{1}{6}. \tag{9}$$

Due to the complexity of expression (3), it cannot be solved analytically. Therefore, in particular, their stability was checked by calculating the numerical values of the equilibrium point z_0 at the values of the parameters $B=0.13; C=0.32; D=0.31; b_1=0.1$. At different values of parameter A, according to condition (9), the equilibrium point α between points α, β $(O<\alpha<\beta)$ is always unstable. Therefore, it repels solutions around itself and it became known that equilibrium point β is stable, that is, it attracts the surrounding solutions (Fig. 2). This, in turn, leads to occurrence of stationary solutions of (2) of regulatory mechanisms of cardiac activity. Therefore, the equilibrium point β is a functional attractor. It can be seen that the solutions of (2) are separated from point A in space of attractors O and B. Sometimes, depending on the parameter values, the equilibrium point β loses its stability and leads to the appearance around it of periodic oscillatory solutions of the Poincare type. This, in turn, means that (2) can represent the periodic oscillation activity of the heart.

3 Results and discussion

The stability of the equilibrium points at certain values of the parameters was checked. According to him, equilibrium point α is always unstable. Initially, the equilibrium point β is stable and with increasing the value of parameter A, a transition to an unstable position was observed in this equilibrium point.

As a result of numerical analysis on a computer, the presence of regular or non-regular oscillatory solutions in the space of attractor B was found due to the loss of stability of the equilibrium point β, and sometimes cases of a sharp falling in non-regular solutions to 0 were identified [9, 10].

4 Conclusions

Summarizing the above considerations, it can be noted that the studied equation (2) has the ability to express a normal state of heart (solutions of periodic oscillations), arrhythmia (solutions with irregular oscillations) and sudden cardiac death (sometimes sudden drop solutions with irregular oscillations to 0 - "the black hole" effect). So, (2) can be used for study the regulatory mechanisms of cardiac activity.

References

1. Young Keul Jeon, Jae Boum Youm, et all. Teaching cardiac excitation-contraction coupling using a mathematical computer simulation model of human ventricular myocytes. Advances in Physiology Education, 44, pp. 323–333. (2020).
2. Y.M. Ishbulatov, A.S.Karavaev, A.R.Kiselev, et al. Mathematical modeling of the cardiovascular autonomic control in healthy subjects during a passive head-up tilt test. Scientific Reports 10, 16525 (2020).
3. S.B. Williams George, D. Smith Gregory, A. Sobie Eric and M. Saleet Jafria. Models of cardiac excitation–contraction coupling in ventricular myocytes // Mathematical Biosciences, Vol. 226(1), pp.1–15. (2010)
4. S.H.Sabzpoushan, A.Ghajarjazy. A Graphical-Based Mathematical Model for Simulating Excitability in a Single Cardiac Cell // Mathematical Problems in Engineering, Vol. 2020, (2020).
5. Satoko Hirabayashi, Masami Iwamoto. Emotion, Respiration, and Heart Rate Variability: A Mathematical Model and Simulation Analyses. Applied Sciences, Vol.9(23), p. 5008; (2019).
6. B.N.Hidirov. Regulation of living systems: qualitative research. Reports of the Academy of Sciences of the Republic of Uzbekistan, No. 8, pp. 12-15, (1998).
7. B.N.Hidirov, M.B.Hidirova, A.R.Shakarov. Qualitative and quantitative analysis of functional differential equations of the Goodwin type. Problems of computational and applied mathematics. Tashkent, Vol. 128, pp. 5-13, (2012).
8. M. Saidalieva, M. B. Hidirova. Qualitative analysis of delay differential equations from medicine. Advances in Mathematics: Scientific Journal Vol. 9(6), pp. 3685–3691. (2020).
9. M. Saidalieva, M. B. Hidirova, A. R. Shakarov, A. M. Turgunov, A. A. Hasanov and Z.Dj.Yusupova. Dynamics of Regulatory Mechanisms of the Human Organism on the Basic Hierarchical Levels of the Organization. IOP Conf. Series: Journal of Physics: Conf. Series Vol. 1210 (2019).
10. M. Saidalieva, M. B. Hidirova, A. M. Turgunov and Z. Dj. Yusupova. Quantitative study of the regulatory mechanisms of cardiac activity and liver function in pathogenesis. IOP Conf. Series: Journal of Physics: Conf. Series Vol.1260 (2019).
11. M. Hidirova, Z. Yusupova. Method of Reduction of the Equation of Mathematical Model of Regulatory Mechanisms of Cardiac Activity. ICISCT 2020 International conference (2020).
12. Z. Dj. Yusupova. Properties of solutions of equation of regulatory mechanisms of cardiac activity. Advanced in Mathematics: Scientific journal, Vol.9(11). pp. 9089–9095. (2020).