



## SYNCHRONIZATION PROBLEM OF THE COUPLED MODIFIED VAN DER POL EQUATIONS IN A MODEL OF THE HEART ACTION

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**ABSTRACT.** In this paper, modified van der Pol equations are considered as a description of the heart action. The physiological model functions over a narrow range of parameters and enables obtaining stable behaviour which is important in the case of a biological system. When some types of pathologies occur in the heart, it is possible to obtain chaotic behaviour. The purpose was to compare how two types of couplings (unidirectional and bidirectional) affect the behaviour of the van der Pol system. The coupling occurs in a healthy conduction system between the SA and AV nodes, however, under some circumstances a pathological coupling may occur. The van der Pol oscillator is a relaxation oscillator which can be synchronized. The synchronization properties of such system have also been studied as part of this paper. A mathematical model was created and numerical analysis of this system were performed in this paper.

### 1. INTRODUCTION

The paper describes research investigating the electrical conduction system of the human heart. In addition to ordinarily working fibres, the heart contains pacemaker centres composed of special cells that resemble embryonic cells. These cells make part of the cardiac conduction system and form the following structures: the sinoatrial node (SA), the atrioventricular node (AV) and the His-Purkinje system, [11]. The key elements of the conduction system, as considered in this paper, are the SA node and the AV node. The two nodes are modelled based on the modified van der Pol oscillator. This model helps to demonstrate phenomena observed in clinical experiments such as Holter recordings. The purpose of this paper was to create a model for describing the behaviour typical for sinoatrial block. The initial cardiac pulse is usually generated in the SA node and carried through the atria to the AV node. When SA block occurs, an electrical impulse is delayed or blocked on the way to the atria, thus delaying atria depolarization. This is different from AV block that occurs in the AV node and delays ventricular depolarization. SA blocks are divided into three main types based on the length of the delay. First degree SA block is characterized by a prolonged conduction time from the SA node to the surrounding atrial tissue. Second degree block can be divided into two types: Wenckebach block and type II. Wenckebach block are characterized by

irregular rhythm. With second degree type I block, the interval is less than twice the minimum length of the period. Type II block shows a regular rhythm which may be either normal or slow. It is followed by an interval equal to a multiple of the period. The conduction across the SA node is normal until up to the time point when the interval occurs and the conduction is blocked. Third degree block is characterized by no atrial activity. The cardiac rhythm is determined by an escape rhythm. In biological systems, it is an extremely important phenomenon of synchronization, it is responsible for many of the periodic processes in the body, e.g. the coupling induced in the pituitary gland is responsible for the production of thyroid hormones. If the two components were not synchronized, the endocrine system could not function properly. The main oscillator in the human body, i.e. the heart, also needs to be properly synchronized. This paper discusses different types of couplings the AV node and SA nodes and their impact on the synchronization of the two oscillators. The analysis of synchronization of various modifications of the van der Pol model has been described in a number of papers. Areas of synchronization near the main parametric resonance and transition conditions from regular to chaotic motion are presented in paper [11]. The phenomenon of complete synchronization within a network of four coupled oscillators is described in [6]. In [9], the authors investigated mechanisms of various bifurcation phenomena observed in Bonhoffer van der Pol neurons coupled through the characteristics of synaptic transmissions with a time delay. Synchronization phenomena in van der Pol oscillators coupled via a time-varying resistor are researched in [10]. However, these papers provide no examples of application of this model for recreating a pathological behavior of the electrical-conduction system of the human heart, and therefore the ranges of parameters considered are wider than those that can be used in medical applications. In [8, 13], the authors showed that two coupled van der Pol oscillators can be used for modelling the behaviour of the cardiac conduction system and they described a heart block as a pathology based on coupled van der Pol oscillators. The van der Pol oscillator provides rich dynamical behavior which we would like to exploit in modeling of the heart action [5] also synchronization phenomena.

**1.1. Mathematical model.** Because each node is a self-exciting pacemaker, it can be described as a relaxation oscillator, i.e. the van der Pol oscillator. The van der Pol and van der Mark model was developed as a model in the electronic circuit theory in 1927:

$$(1.1) \quad \ddot{x} + a(x^2 - 1)\dot{x} + x = 0, \quad a > 0,$$

where  $a(x^2 - 1)$  is a damping coefficient given as a function of  $x$ , negative for  $|x| < 1$  and positive for  $|x| > 1$ . The Eq. (1.1) posses a periodic solution that attracts other solution except the trivial one at the unique equilibrium point  $x = \dot{x} = 0$ . The phase portraits depend on  $a$ . If  $a = 0$ , there is a harmonic oscillator and all solutions are periodic with  $x(t) = a_1 \cos t + a_2 \sin t$ . If  $a > 0$ , there is a stable limit cycle but if  $a$  increasing the nonlinearity of system also increasing. The dynamics of Eq. (1.1) is well known in the literature [1, 2, 4]. The van der Pol model needs to be changed so as to reproduce the actual features of the action potential. Postnov [7] introduced modifications that maintain the required structure of the phase space. More precisely, he substituted a linear term by a nonlinear cubic force called the Duffing term.

$$(1.2) \quad \ddot{x} + a(x^2 - \mu)\dot{x} + \frac{x(x+d)(x+2d)}{d^2} = 0,$$

where  $a, \mu, d$  are positive control parameters.

This model can be considered as a SA or AV node model. The mutual interaction of a limit cycle present around an unstable focus with a saddle and a stable node is the main property of a modified relaxation oscillator. As a result, the refraction period and nonlinear phase sensitivity of the action potential of node cells are reproduced correctly. A solution of this equation in time presents the action potential whereas a solution in velocity allows to obtain very important phase portrait. It can be easily seen that the main qualitative difference between Eqs. (1.1) and (1.2) is the emergence of two additional steady states,  $x_2^* = -d$  and  $x_3^* = -2d$ . As before,  $x_1^* = 0$  is an unstable node or focus surrounded by a unique stable limit cycle,  $x_2^* = -d$  is a saddle and  $x_3^* = -2d$  is a focus or a node and can be either stable or unstable, depending on the sign of  $4d^2 - \mu$ . In the case considered by Postnov [7], the first steady state is an unstable focus, while the third one is a stable node which attracts all solutions, starting from the right-hand side of the stable manifold of the saddle  $x_2^*$ . However, in the considered model (1.2) it is difficult to regulate the location of steady states in the phase space, so to reproduce the heart behavior new parameter  $e$  is introduced. It should be noted that this modification does not affect the phase portrait, while the location of steady states can be modified. In order to simplify a frequency regulation and obtain the proper timescale the  $ed$  factor in the denominator is substituted with the independent coefficient  $f$  which corresponds to the frequency of harmonic oscillator [3]. The final version of the model is given in its two variable first-order form [3, 12]:

$$(1.3) \quad \begin{aligned} \dot{x} &= y, \\ \dot{y} &= -a(x^2 - 1)y - fx(x + d)(x + e). \end{aligned}$$

The van der Pol equation has been considered as one node so that a coupled system of two nodes has been generated. This model includes both the SA and AV node. The created system that we analyze is given as follows:

$$(1.4) \quad \begin{aligned} \dot{x}_1(t) &= y_1(t) + (k - k_1)x_1(t - w_1) - kx_1(t) + k_1x_1(t - w_2), \\ \dot{y}_1(t) &= -a_1(x_1(t)^2 - 1)y_1(t) - f_1x_1(t)(x_1(t) + d_1)(x_1(t) + e_1) \\ &\quad + s_1(x_2(t) - x_1(t)), \\ \dot{x}_2(t) &= y_2(t), \\ \dot{y}_2(t) &= -a_2(x_2(t)^2 - 1)y_2(t) - f_2x_2(t)(x_2(t) + d_2)(x_2(t) + e_2) \\ &\quad + s_2(x_1(t) - x_2(t)), \end{aligned}$$

where  $x_1$  -potential of SA node,  $x_2$  - potential of AV node,  $y_1, y_2$  - currents,  $a_1, a_2, f_1, f_2, d_1, d_2, e_1, e_2$  are control parameters.  $k, k_1, s_1, s_2$  - coupling coefficients and  $w_1, w_2$  - delays (In case in which there is a feedback we use a delay because original signal of SA node is modified by signal from flutter wave with delay. Delay is caused by longer way of signal of the flutter wave. Delay is only in  $x_1$  variable because in this pathological behaviour there is a flutter wave only in SA node).

The coupling coefficients correspond to the 'power' of feedback or unidirectional or bidirectional coupling. Depending on the tissue by which the pulse passes the value of the coupling ratio may vary. In our system, the feedback describes the situation when the output from the system influences the input and modifies the system's action.

Parameter's values for the modified van der Pol oscillator were chosen such that the oscillation's frequency corresponds to a real frequency of SA and AV nodes. The setup of particular parameters and acceptable variability ranges are briefly presented below. This information is essential for

examining stability of our setup because without such limitations the system could have completely different properties and would not recreate physiological properties. Modification of the parameter  $a$  value increases time intervals between pulses but also changes their shapes. This behavior is inconsistent with physiological observations. This disadvantage of the van der Pol oscillator is related to the phase space structure. Modification of the  $e$  parameter of the node location influences the distance between consecutive potential needles without changing their shapes. This means that the mutual position of a saddle and a node influences the time of spontaneous depolarization which is one of the physiological mechanisms of a regulation of the action potential generation frequency. Dependency of the considered oscillator on the parameter  $e$  is nonlinear, [3]. Saturation of the curve is consistent with physiological observations because of the fact that heart's ability to increase a rhythm frequency decreases for higher rhythm frequencies. The parameter  $e$  plays a major role in the validation process of the model. The parameter  $a$  is in the range  $[0.5, 6]$ , the parameter  $e$  belongs to the interval  $[7, 12]$  and the parameter  $f$  may change only in the small range  $[2.5, 3]$ . A more detailed description of the physiological interpretation of the parameters can be found in the work [12].

The system with a sum of delays with feedback describes the SA block in which the potential wave is not conducted in a physiological way. The action potential is generated in the SA node, however, it is not conducted normally. Instead, it forms a re-entry wave (which is delayed relative to the original potential because it circulates around the SA node before it is conducted to the next structure). There can be more than one non-conducted potential and this the model includes two feedbacks with delay. These terms are added to the first van der Pol equation for the SA node. This is typical behaviour of the Weckenbach block. The Weckenbach block is caused by a disease process involving the sinus node and atrial muscle which gives rise to abnormal conduction in the sinoatrial node. There are situations when output potential from SA node influences the input potential and modifies the action of the system. The two values of the coupling coefficients  $k_1$  and  $k_2$  take into account the transition of wave through various cardiac tissues.

The coupling between these two nodes can be either unidirectional or bidirectional. In this case, the coupling is unidirectional, i.e. it is from the SA node to the AV node ( $s_2 \neq 0, s_1 = 0$ ) or from the AV node to SA node (non-physiological behaviour  $s_1 \neq 0, s_2 = 0$ ).

**1.2. The problem of synchronization.** The behaviour of the cardiac pacemaker cells resembles that of a relaxation oscillators. A characteristic feature of a relaxation oscillator is that it can be synchronized by an external signal if the latter has a periodicity is not significantly different from the spontaneous frequency of the oscillator [5]. Synchronization, defined as an adjustment of rhythm due to weak interaction, is one of the most interesting features displayed by coupled oscillators. In this paper, we have investigated a phenomenological heartbeat that consists of two coupled van der Pol oscillators.

## 2. NUMERICAL ANALYSIS

It will be subjected to numerical analysis model that reproduces the physiological behavior of the potentials occurring in a conducting system of the heart. A system with delayed feedback describes various pathologies of the heart action, e.g. the SA block. When the coupling  $s_2$  is added, the SA node affects the AV node rhythm. This is physiological behaviour. Adding  $s_1$  causes pathological behaviour that we get re-entry wave in our system. This is typical of the WPW syndrome. After including feedback and delay, the time series looks like in the Figure 1. The top

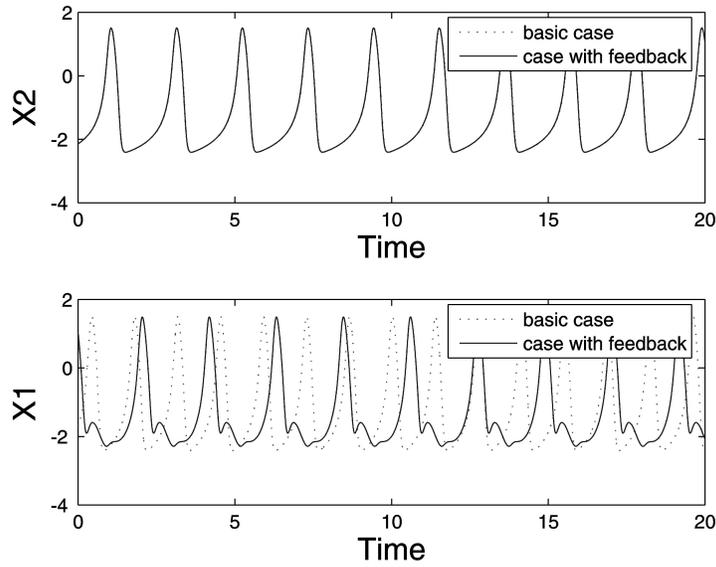


FIGURE 1. Time series a) model without feedback, b) with feedback

graph shows the initial model with no feedback. The bottom graph in Figure 1 shows a modified model with feedback.

The parameters  $k = 1$ ,  $k_1 = 2.85$  and  $w_1 = 0.75$ ,  $w_2 = 0.25$  (delays in our research are constant) have the following values, while the other parameters are reference parameters:  $a_1 = a_2 = 5$ ,  $f_1 = f_2 = 3$ ,  $d_1 = d_2 = 3$ ,  $e_1 = 7$ ,  $e_2 = 4.5$ . The selection of appropriate parameters was done after the verification of the Eq. (1.3) by Grudziński in [3]. Parameters values for mvdP were chosen so that the oscillations frequency corresponds to real frequencies of the SA and AV nodes. In the time series of the modified model with feedback, there is a 'delayed impulse'. The period of this oscillator is almost two times longer than that in the reference model (the potential period for a single node model of an electrical conduction system with no coupling and feedback equals about 1.4), similarly to the second type of the SA block. This is one of the mechanisms causing bradycardia. If the SA nodal impulses occur at a rate less than 60 beats/minute, the heart rhythm is known as bradycardia (normal sinus rhythm: 60-100 beats/minute). Re-entries play an important role in the formation of cardiac arrhythmias. They are modelled using a feedback term which is added to the van der Pol equation. The use of certain values for coupled terms enables simulating the circulation of reentry waves which play an important role in generating pathological heart rates. Formation of the reentry wave is a result of time differences in repolarisation and refraction between abutting cells of the cardiac muscle. They can evoke a local delay and create locally unidirectional block which fosters the pronation of the wave of conduction. Now we change in our system one of the coupling coefficients  $k_1$ . The results in a significant difference in the time series of the modified van der Pol's equations. If  $k_1 = 2.5$  is present, a kind of tachycardia is obtained. The amplitude death can be understood as full heart block and it is appeared for  $k_1 = 3$ , as shown in Figure 2. The top graph in Figure 2 shows that curve of  $x_2$  is not changed because the feedback directs only variable of  $x_1$  (feedback is added to first part of system). We can observe changes of

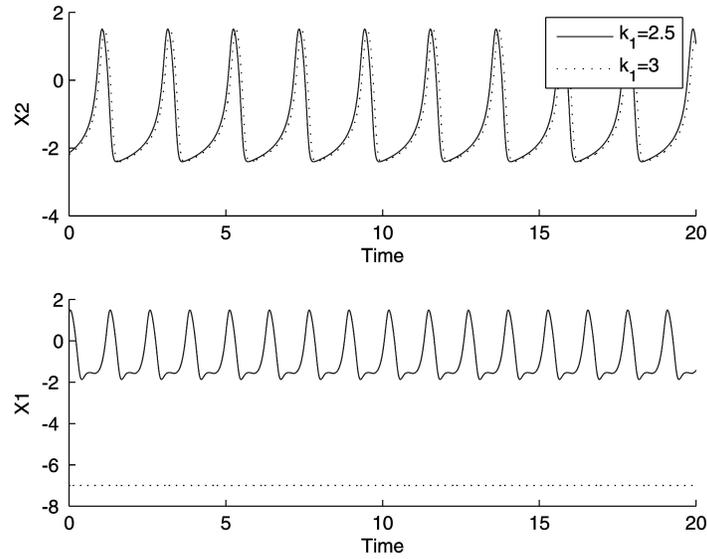


FIGURE 2. Time series: Model with feedback, where  $k_1$  is changed

the behaviour of action potential under the influence of the addition of the feedback in the bottom graph in Figure 2.

Third degree of SA block is characterized by no atrial activity. No impulses are conducted to the AV node. As a result, the AV node may take over the function of pacemaker. In order to reproduce the escape rhythm,  $s_1$  has to be added to our system, Figure 3. The graphs show that  $x_1$  and  $x_2$  have a similar period length, but there is no phase synchronization. Figure 3 shows a part of anti-phase synchronization, the curves have a different shape. The curve  $x_1$  has a breakdown curve which shows that oscillations have a more and less sensitive phase (time of refraction). For larger  $s_1 = 5$ , the death amplitude can also be observed. This interesting behaviour has been observed for other large values of at least one coupling coefficient. However, we are not sure as to its nature.

There is no changes of variable of  $x_2$  because in this case, there is only unidirectional coupling. If the coupling  $s_1$  is introduced to our system, it means that the  $x_2$  directs the  $x_1$ . This is the reason why there is no changes in the behavior of the variable  $x_2$ .

If the physiological coupling between nodes is considered, than the coupling  $s_2$  is introduced to our system. It means that the SA node directs the AV node (If the coupling  $s_2$  is introduced to our system, it means that the  $x_1$  directs the  $x_2$ . This is the reason why there is no changes in the behavior of the variable  $x_1$ ). If  $s_2$  is small, the result is similar to the reference value. If its value is larger (e.g. [12]), the system strives to complete synchronization in phase with  $x_1$ . If  $s_2$  is larger, full in-phase synchronization is obtained as shown in Figure 4. This causes the attempt of fitting the AV frequency to the SA frequency which slows down the heart rate.

Next numerical analysis has been prepared for a model with the parameters  $k = 1, k_1 = 2.85$  and  $w_1 = 0.75, w_2 = 0.25$  and the other parameters are identical to those in the reference system.

The addition of coupling to  $y_1$  term in a model with feedback enables modelling a re-entry wave which causes an exceptional situation in that the AV node is the master for the SA node. Such situation takes place in case of WPW syndrome. Slowing the oscillations down caused by

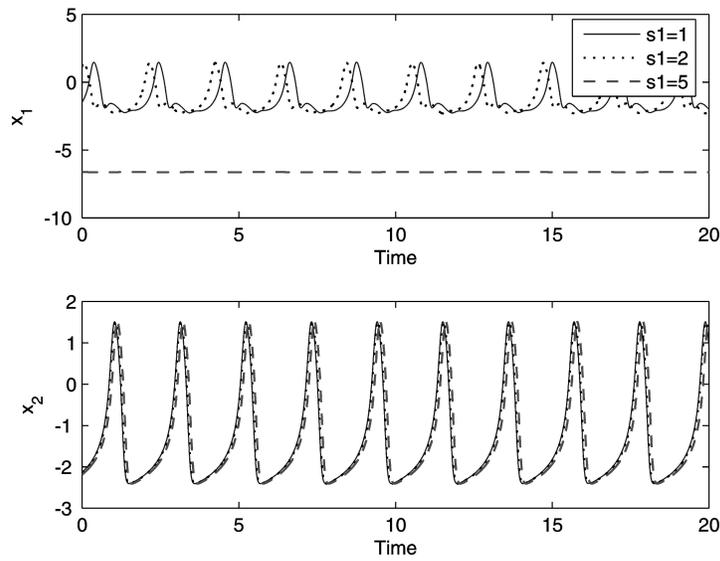


FIGURE 3. Time series: Model with feedback and coupling coefficient  $s_1$

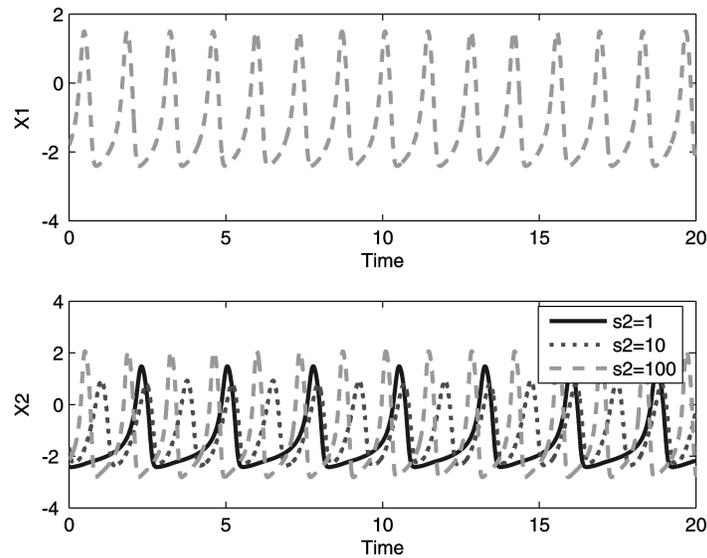


FIGURE 4. Time series: physiological coupling between nodes

feedback and addition of  $s_1$  coupling we obtain the aperiodic behaviour. The big arrhythmia occurs. From the medical point of view it resembles atrial fibrillation. The oscillator begins to behave aperiodically in an attempt to adjust its frequency to the frequency of the AV node. The oscillation period tends to be shorter despite no periodic behaviour, as shown in Figure 5. The amplitude changes with time as illustrated in the graph  $x_1$  in Figure 5. If  $s_1$  is large, our system attempts

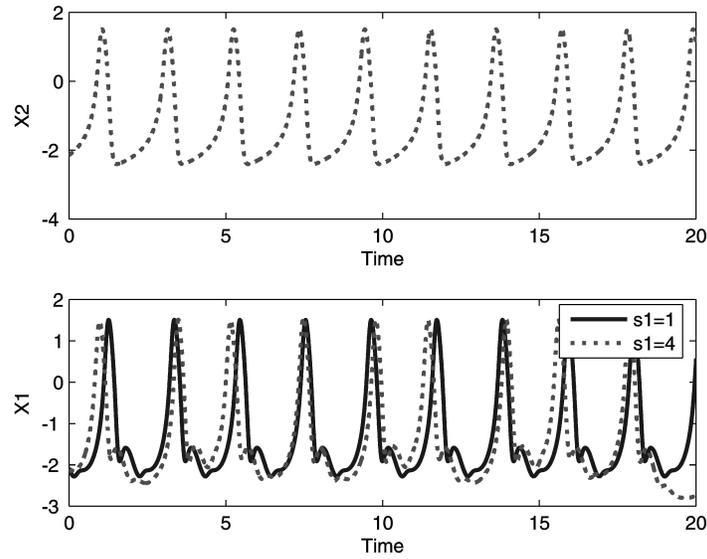


FIGURE 5. Time series: pathological coupling between nodes

to achieve synchronization in phase, but the curve  $x_1$  has a different shape. The system is phase-sensitive, and that depending on phase, excitation (here a kind of wave which is generated in coupling process) may change the length of the potential period. The results of this analysis have been confirmed experimentally.

Figure 6 and 7, plots of synchronization for the model without feedback show that for system with the coupling  $s_2$ , synchronization of the system is greater than for a system with the coupling  $s_1$ . Similar results have been obtained for a system with feedback.

Last we studied the influence of the bidirectional coupling for behaviour of our model. It would seem that the bidirectional coupling should operate so that when we enter it 1 : 1 between the node SA (60-100 bmp) and the AV node (40-60 bmp), the rhythm of the sinus node should be slowed down, while the rhythm of the AV node should accelerate.

In the model without feedback, with  $s_1 = 20$  and  $s_2 = 1$ , aperiodic potential  $x_1$  is obtained – typical arrhythmia, Figure 8. There is no synchronization for these parameters. However, with smaller values of  $s_1$ , a part of synchronization can be found in the system. Large values of  $s_1$  cause the most significant changes in the  $x_1$  signal.

An interesting behaviour is obtained with the same model, however, with feedback as shown in Figure 9. The behaviour of the curve  $x_2$  is similar to that shown in Figure 8. There is periodic behaviour and small changes in the the course of chart. But the time series for  $x_1$  is highly exceptional. The length of the period has increased significantly. The signal does not exhibit periodic behavior for large values of  $s_1$ . In this case, the system is characterized by two types of feedback, where one of them is unidirectional (adding to the first equation of our model) and the other one is bidirectional. We can see a strong activity of feedback, which is posed in the model. As can be seen in Figure 1, this type of feedback with delay causes the system to continue to behave periodically, while the oscillation period is considerably longer and the shape of oscillations is changed.

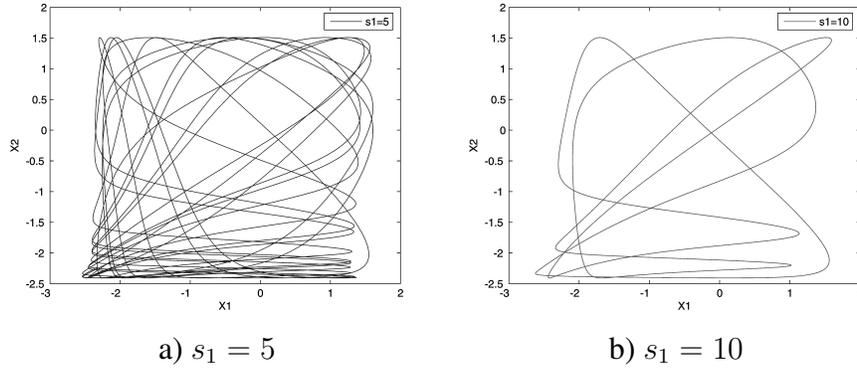


FIGURE 6. Synchronization plot for unidirectional cases: a)  $s_1 = 5$  and b)  $s_1 = 10$ , initial conditions:  $[0.1; 0.1; 0.1; 0.1]$

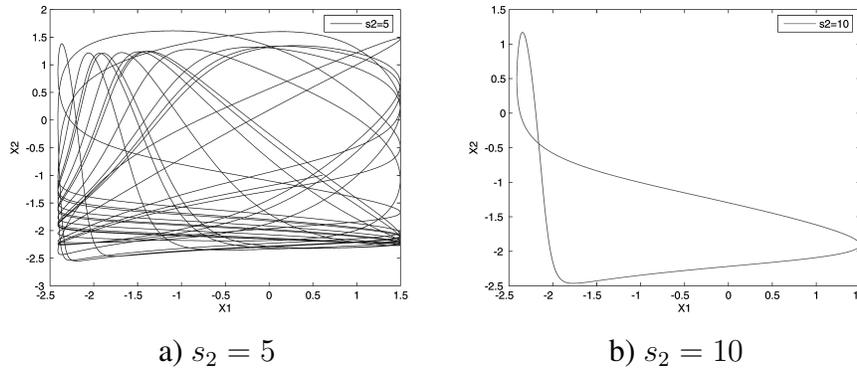


FIGURE 7. Synchronization plot for unidirectional case:  $s_2$

By adding the bidirectional coupling, the system has two couplings, where the bidirectional coupling strengthens the feedback in the system, leading to significant changes in the behavior of the system. The length of the oscillation period varies with time and lasts up to 3 times longer compared to the reference model and the strong oscillatory nature of the system disappears. It is worth noting that with lower values of  $s_1$  and  $s_2$  the system behaves periodically, even though the period of oscillation is longer (identical to that with a single feedback).

Such dynamics of the action potential can be observed in the presence of bradycardia due to conduction block in the conduction system of the heart. Feedback occurring in the mathematical model corresponds here re-entry waves generated by the closure the impulse road by the occurrence of the block of the heart. Often with this type of block coexist disorder in the relationship between nodes. In this case, the AV node can start to work just as a pacemaker (SA node), hence we introduce here also additionally bidirectional coupling. It is worth noting that during bradycardia, heart rhythm must be slower than typical and does not have to be regular.

### 3. CONCLUSIONS

The analyzed system is stable and not easy to put out of periodic behaviour. The setup of a single delay feedback was characterized by low variability and strong oscillatory nature. It is worth noting

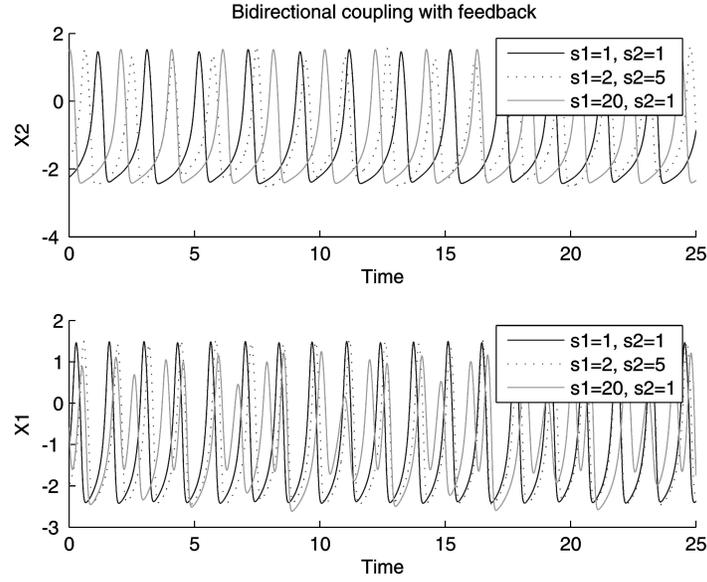


FIGURE 8. Time series: bidirectional coupling between nodes

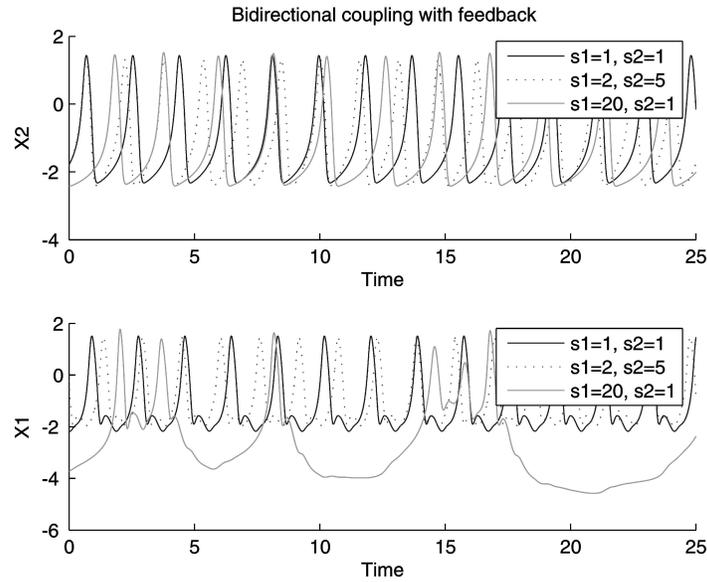


FIGURE 9. Time series: bidirectional coupling between nodes

that the system discussed functions over a very narrow range of control parameters. If we add to the system proposed by us a number of couplings in order to reproduce the phenomena occurring in the conducting system, this will greatly influence the behaviour of the oscillator. It can cause the extinction of oscillations as well as non-periodic behaviour. The ability to recreate physiological behaviour is extremely important, especially because such behaviour includes disorders whose sources lie in the complex processes of the conducting system. This couplings of mathematical

system interfere in similar way in a work of conduction system of the heart (SA block, AV block, bradycardia, WPW syndrome). Synchronization in the investigated cases is rarely in-phase, often in anti-phase. Bidirectional coupling should be used to describe the physiological behaviour of the conduction system because only this way we can take into account the effect of the AV node as a delay element (coupling  $s_1$ ). In this study, the model correctly reproduces pathologies of the heart action such as SA block or one of arrhythmias. However, it should be noted that this is a phenomenological model, four-dimensional, so that the results are as accurate as possible using a simple model to describe the potential found in one of the most complex biological oscillators. In further research it is planned to perform the bifurcation analysis for selected, more essential, parameters. This will allow for a better understanding of the dynamics of examined model.

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