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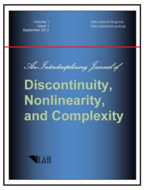

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Synchronization of the Cardiac Pacemaker Model with Delayed Pulse-coupling

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Abstract

We reconsider the C. Peskin model of the cardiac pacemaker assuming that pulse-couplings are delayed. Sufficient conditions for synchronization of identical and non-identical oscillators are obtained. The results are demonstrated with numerical simulations.

1 Introduction

A specialized bundle of about 10000 neurons located in the upper part of the right atrium of the heart is known as the sinoatrial node. It fires at regular intervals to cause the heart beat with a rhythm of about 60 to 70 beats per minute for a healthy, resting heart. The electrical impulse from the pacemaker triggers a sequence of electrical events in the heart to control the orderly sequence of muscle contractions that pump the blood out of the heart. That is why it is called the *cardiac pacemaker* in the literature. The cells of the sinoatrial node are able to depolarize spontaneously toward the threshold firing, and then recover [1]. The electrical activity of the cardiac pacemaker produces a strong pattern of voltage change. While it is the norm for nerve cells that they require a stimulus to fire, cells of the cardiac pacemaker can be considered to be “self-firing”. It repetitively goes through a depolarizing discharge and then recover to fire again. This action is analogous to a relaxation oscillator in electronics. The circuit involves a capacitor which is charged by the energy of a battery (the membranes of the sinoatrial node and the ion transport processes play the role) and a resistor which controls the flashing rate of the light. In the case of the sinoatrial node, there is an input from the physiology of the body related to oxygen

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demand and other factors which control the rate of firing of the sinoatrial node and hence the heart rate. The question naturally arises how the neurons organize their *firing in unison*. The simplest explanation was that the fastest neuron drives all the others bringing them to the threshold. If it were the case, then the injury of a single cell could have significantly changed the frequency of the heart beat. To avoid this important shortcoming, in paper [2] C. Peskin proposed a model of a cardiac pacemaker, where signals of fires arise not from an outside stimuli, but originate in the population of cells itself. Moreover, it was proposed that a cardiac pacemaker is a population of neurons with weak couplings such that synchrony emerges as a result of the interaction of all cells, rather than a single cell domination. Well known conjectures of self-synchronization were formulated and solutions of these conjectures for *identical oscillators* [2,3] stimulated intensive investigations [4]– [12].

In papers [13]– [15], we have introduced a new method for investigation of biological oscillators. The method seems to be universal to analyze integrate-and-fire oscillators. In particular, we have solved the Second Peskin conjecture in [13, 14]. It was proved that an ensemble of arbitrary number of oscillators synchronizes even if they are *not quite identical*. In the present article we extend the approach to the model with delayed pulse-coupling. Conditions are found, which guarantee synchronization of the model. Our system is different than that in [5], since we suppose that the pulse-coupling is instantaneous, if oscillators are close to each other and are near threshold. In next our papers, we plan to consider other models, varying types of the delay involvement, as well as inhibitory models such that analogues of results in [5] and [16] can be obtained. Moreover, we plan to develop for these systems the theory of the bifurcation of periodic solutions. Some of open problems are discussed in the conclusion part of the paper. The method of the analysis of non-identical oscillators is based on results of the theory of differential equations with discontinuities at non-fixed moments [17]- [27].

Delays arise naturally in many biological models [28]. In particular, they were considered in firefly models [29] as delay between stimulus and response, and in continuously coupled neuronal oscillators [30]. Authors of [5] considered the phenomenon for the analysis of Mirollo and Strogatz in such a way that identical oscillators were investigated. The dynamics of two oscillators were discussed mathematically, and a multi-oscillatory system was analyzed by using computer simulations. It was found that the excitatory model of two units “can get only out-of-phase synchronization since in-phase synchronization proved to be not stable.” In paper [6] a model without a leakage was discussed, that is, oscillators increase at a constant rate between moments of firing. It was found that a periodic solution is reached after a finite time. Consequently, research of integrate-and-fire models, which admit delays and fire in unison is still on the agenda.

2 The couple of identical oscillators

Let us start with the analysis of two identical oscillators, which satisfy, if they do not fire, the following differential equations

$$x_i' = S - \gamma x_i, \tag{1}$$

where $0 \le x_i \le 1, i = 1,2$. It is assumed that S, γ are positive numbers and $\kappa = \frac{S}{\gamma} > 1$. In (1) each $x_i, i = 1,2,$ is a voltage-like state variable, S is an external stimulus, and γ is the leakage coefficient.

When $x_j(t) = 1$, then the oscillator fires, $x_j(t+) = 0$. The firing changes the value of the another oscillator, x_i, such that

$$x_i(t+) = 0, \tag{2}$$

if $x_i(t) \ge 1-\varepsilon$, and

$$x_i(t+\tau+) = \begin{cases} x_i(t+\tau)+\varepsilon, \text{if} x_i(t+\tau) < 1-\varepsilon, \\ 0, \text{ otherwise}, \end{cases} \tag{3}$$

otherwise.

Thus, from (3) it implies that $t+\tau$ is a firing moment for x_i, if the jump makes the value of the oscillator not smaller than 1.

In paper [2], the following coupling mechanism was introduced. If oscillator x_j fires at the moment t, then the firing changes the value of the another oscillator, x_i, such that

$$x_i(t+) = \begin{cases} x_i(t)+\varepsilon, \text{if } x_i(t) < 1-\varepsilon, \\ 0, \text{ otherwise.} \end{cases} \tag{4}$$

That is no delay was assumed for the pulse-coupling.

In what follows, assume that

$$\frac{\kappa-1}{\kappa-1+\varepsilon} < \mathrm{e}^{-\gamma\tau}. \tag{5}$$

We have that

$$x_i(s) = x_i(t)\mathrm{e}^{-\gamma(s-t)} + \int_t^s \mathrm{e}^{-\gamma(s-u)} S du$$

near t, where t is assumed again the firing moment for x_j, and

$$x_i(s) \le (1-\varepsilon)\mathrm{e}^{-\gamma\tau} + \kappa(1-\mathrm{e}^{-\gamma\tau}).$$

From (5) it implies that if $x_i(t) < 1-\varepsilon$, then $x_i(s) < 1$, for all $s \in [t,\ t+\tau]$. In other words, the oscillator x_i does not achieve the threshold within interval $[t,\ t+\tau]$, if the distance of $x_i(t)$ to threshold is more than ε. This is important for the construction of the prototype map, and makes a sense of condition (3).

One must emphasize that couplings of units are not only delayed in our model. By (2) oscillators interact instantaneously, if they are near the threshold. This assumption is natural as firing provokes another oscillator, which is being close to the threshold "is ready" to react instantaneously. Otherwise, the interaction is retarded.

Next, we shall construct the prototype map. Fix a moment $t=\zeta$, when x_1 fires, and suppose that oscillators are not synchronized. In interval $[\zeta, \zeta+\tau]$ the oscillator x_2 moves according to the law $x_2(t) = x_2(\zeta)\mathrm{e}^{-\gamma(t-\zeta)} + \int_\zeta^t \mathrm{e}^{-\gamma(t-u)} S du$, and

$$x_2(\zeta+\tau) = [x_2(\zeta)-\kappa]\mathrm{e}^{-\gamma\tau} + \kappa. \tag{6}$$

Let us, firstly, handle the problem in the case that $x_2(\zeta+\tau)+\varepsilon < 1$. One can verify that this is true if $x_2(\zeta) < \bar{v}$, where $\bar{v} = \mathrm{e}^{\gamma\tau}(1-\varepsilon-\kappa)+\kappa$. It is important that $\bar{v} < 1-\varepsilon_1$, where $\varepsilon_1 = \varepsilon\mathrm{e}^{\gamma\tau}$. Take $\tau > 0$ so small such that the inequality

$$\mathrm{e}^{-\gamma\tau} > \varepsilon \tag{7}$$

holds. From (7) it implies that $\varepsilon_1 < 1$. If we denote by $t=\eta$ the firing moment of x_2, then one can reveal that

$$x_2(\eta) = [x_2(\zeta+\tau)+\varepsilon]\mathrm{e}^{-\gamma(\eta-\zeta-\tau)} + \kappa[1-\mathrm{e}^{-\gamma(\eta-\zeta-\tau)}].$$

The equation $x_2(\eta) = 1$ implies the following

$$\mathrm{e}^{-\gamma(\eta-\zeta)} = \frac{1-\kappa}{x_2(\zeta)-\kappa+\varepsilon_1}. \tag{8}$$

It follows from $x_1(\eta) = \kappa[1-\mathrm{e}^{-\gamma(\eta-\zeta)}]$ that

$$x_1(\eta) = \kappa\frac{1-(x_2(\zeta)+\varepsilon_1)}{\kappa-(x_2(\zeta)+\varepsilon_1)}. \tag{9}$$

Introduce the following map

$$L_D(v,\varepsilon) = \kappa\frac{1-(v+\varepsilon_1)}{\kappa-(v+\varepsilon_1)}, \text{ for } 0 < v < \bar{v}, \tag{10}$$

such that $x_1(\eta) = L_D(x_2(\zeta)), \varepsilon)$.

Next, let us consider the case that $1 \le x_2(\zeta+\tau)+\varepsilon$. By (3) we have that $\eta = \zeta+\tau$, and $x_1(\eta) = \kappa[1-\mathrm{e}^{-\gamma\tau}]$. Set $\tilde{v} = \kappa[1-\mathrm{e}^{-\gamma\tau}]$, and introduce

$$L_D(v,\varepsilon) = \tilde{v}, \text{ for } \bar{v} \le v < 1-\varepsilon. \tag{11}$$

In what follows we assume that

$$\mathrm{e}^{\gamma\tau} < \sqrt{\frac{\kappa}{\kappa-1+\varepsilon_1}}. \tag{12}$$

Now, we will define an extension of L_D on $[0,1]$ in the following way. Let

$$\omega = \kappa\frac{1-\varepsilon_1}{\kappa-\varepsilon_1}. \tag{13}$$

One can see that $1-\varepsilon < \omega < 1$, provided that

$$\mathrm{e}^{\gamma\tau} < \frac{\kappa}{\kappa-1+\varepsilon_1}. \tag{14}$$

In the sequel, we assume that the number ε is sufficiently small such that (5) implies (14). We set $L_D(0,\varepsilon) = \omega$, and define $L_D(v,\varepsilon) = 0$, if $1-\varepsilon \le v \le 1$.

The derivatives of the map in $(0,\bar{v})$ satisfy

$$L_D'(v,\varepsilon) = \kappa\frac{1-\kappa}{(\kappa-(v+\varepsilon_1))^2} < 0, \tag{15}$$

and

$$L_D''(v,\varepsilon) = 2\kappa\frac{1-\kappa}{(\kappa-(v+\varepsilon))^3} < 0. \tag{16}$$

It is possible to verify that there is a fixed point of the map,

$$v^* = (\kappa-\frac{\varepsilon_1}{2}) - \sqrt{\kappa^2-\kappa+\frac{\varepsilon_1^2}{4}}, \tag{17}$$

and that

$$L_D'(v^*,\varepsilon) < -1. \tag{18}$$

Stated in other words, the fixed point v^* is a repellor. The inequality $v^* < \bar{v}$ holds, if the condition (12) is valid, and consequently, all our previous evaluations are justified.

Suppose, additionally, that

$$\kappa(1-\mathrm{e}^{-\gamma\tau}) < \frac{\varepsilon\kappa}{\kappa-1+\varepsilon} - \varepsilon\mathrm{e}^{\gamma\tau}. \tag{19}$$

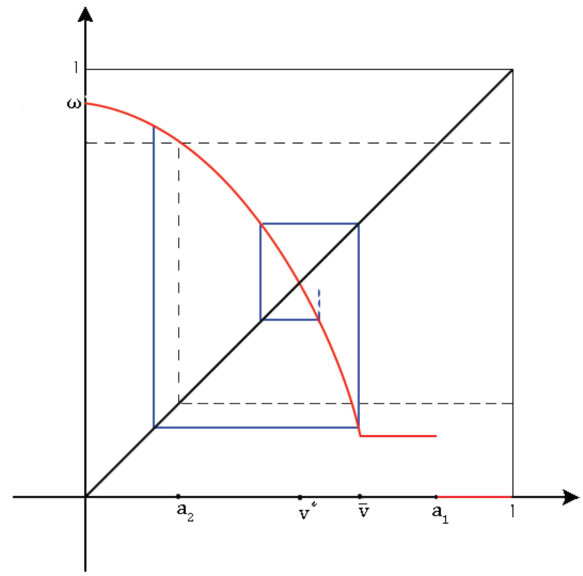

Fig. 1 The graph of map L_D in red, fixed point v^*, and stabilized trajectory are seen.

Denote by $v = a_2$ the solution of the equation $L_D(v,\varepsilon) = 1-\varepsilon$. We find that $a_2 = \frac{\varepsilon\kappa}{\kappa-1+\varepsilon} - \varepsilon e^{\gamma\tau}$. By means of the last inequality we have $\tilde{v} < a_2$.

We call τ the *small delay* since (5), (7), (12), (14) and (19) are assumed to be true. The graph of L_D (in red) under above mentioned conditions is illustrated in Figure 1. One can see that L_D is a piecewise map. This is a curios fact, since in previous our papers for non-delayed pulse couplings or continuous couplings, the prototype map was continuous. Obviously, the discontinuity of the map gives more possibilities for various dynamical collective effects of integrate-and-fire oscillators.

To emphasize a significance of this map for the present analysis, let us see how iterations of it can help to observe the synchronization. Fix $t_0 \geq 0$, a firing moment, such that $x_1(t_0) = 1$ and $x_1(t_0+) = 0$. When the couple x_1 and x_2 are not in synchrony, there exists a sequence of moments $t_0 < t_1 < \ldots$ such that x_1 fires at t_i with even i and x_2 with odd indices. Denote $u_i = x_1(t_i)$, if i is odd, and $u_i = x_2(t_i)$, if i is even. One can easily see that $u_{i+1} = L_D(u_i,\varepsilon), i \geq 0$. The pair synchronizes if and only if there exists $j \geq 1$ such that $x_1(t) \neq x_2(t)$, if $t \leq t_j$, and $x_1(t) = x_2(t)$, for $t > t_j$. In particular, both oscillators have to fire at t_j. In other words, the inequalities $1-\varepsilon \leq u_{j-1} < 1$ are valid. In particular, we have that $L_D(0) = \omega$ satisfies this condition. In the same time, if $1-\varepsilon_1 \leq u_{j-3} \leq 1$, then $u_{j-2} = 0 = L_D(u_{j-3})$ and $1-\varepsilon < u_{j-1} = \omega < 1$ again. That is, we have found that if there exists an integer $k \geq 0$ such that $1-\varepsilon \leq L_D^k(v) \leq 1$, then the motion $(x_1(t), x_2(t))$ with $x_1(t_0+) = v, x_2(t_0+) = 0$, synchronizes at the $k-$th firing moment. Conversely, if a motion $(x_1(t), x_2(t))$ synchronizes, then one can find a firing moment, t_0, such that $x_1(t_0+) = 0, x_2(t_0+) = v, v \in [0,1]$, and a number k with the property that $1-\varepsilon \leq L_D^k(v) \leq 1$.

Thus, the last discussion confirms that the analysis of synchronization is consistent fully with the dynamics of the introduced map $L_D(v,\varepsilon)$ on $[0,1]$, and the map L_D can be applied as the main instrument of the paper. That is why, we use this function as a prototype map in our investigations.

Now, by the help of the properties of the map L_D, and analyzing self-compositions of the map, one can easily attain that for all $k \geq 0$ functions L_D^k have only one fixed point, v^*, and $|[L_D^k(v^*,\varepsilon)]'| > 1$. We skip the discussion as it is respectively simple, and requests a large place. Since all the maps L_D^k have one and the same fixed point, v^*, there is not a $k-$periodic motion, $k > 1$, of the map. Consequently, for arbitrary point $v \neq v^*$ one has a stabilized trajectory as presented in Figure 1. The couple synchronizes when $L_D^k(v,\varepsilon) \geq 1-\varepsilon$.

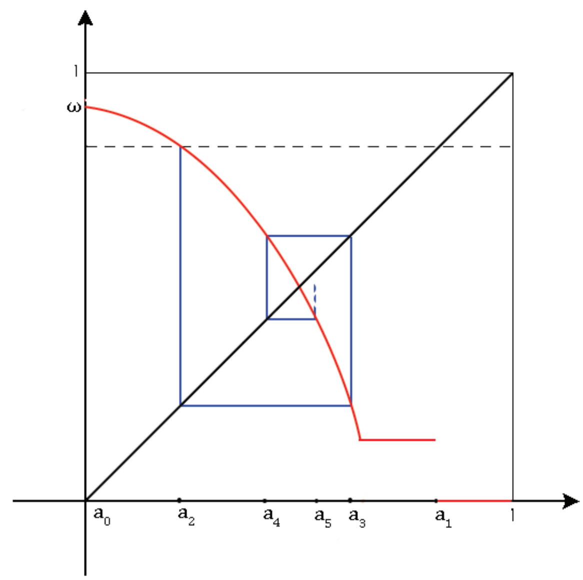

Fig. 2 Boundaries, a_i, of rate intervals are seen.

Next, we investigate the rate of synchronization. Set $a_0 = 0, a_1 = 1 - \varepsilon$ and $a_{k+1} = L_D^{-1}(a_k), k = 2, 3, \ldots$ (See Figure 2).

Denote by S_k the subset of the interval $[0,1]$, consisting of the points v which are synchronized after exactly k iterations of the map L_D. It is easy to verify that $S_0 = [a_1, 1], S_1 = [a_0, a_2]$ and $S_k = (a_{k-1}, a_{k+1}]$, if $k \geq 3$, is an odd positive integer, and $S_k = [a_{k+1}, a_{k-1})$, if $k \geq 2$, is an even positive integer. One can observe that $a_k \to v^*$ as $k \to \infty$. We shall call $S_k, k \geq 0$, the rate intervals.

From the discussion mentioned above it follows that no finite time is available such that *all* points of the unit square synchronize at that moment. The closer v is to the equilibrium v^*, the later is the moment of synchronization.

Set $T = \frac{1}{\gamma} \ln \frac{\kappa}{\kappa - 1}$ and denote by $\tilde{T}$ the time needed for solution $u(t, 0, v^*)$ of the equation $u' = S - \gamma u$, to achieve threshold. Since all oscillators fire within an interval of length T and the distance between two firing moments of an oscillator are not less than $\tilde{T}$, we can conclude the validity of the following theorem.

Theorem 1. *Assume that the conditions* (5), (7), (12), (14) *and* (19) *are valid. If* $t_0 \geq 0$ *is a firing moment,* $x_1(t_0) = 1, x_1(t_0+) = 0$, *and* $x_2(t_0+) \in S_m$ *for some natural number* m, *then the couple* x_1, x_2 *of continuously coupled identical biological oscillators synchronizes within the time interval* $[t_0 + \frac{m}{2}\tilde{T},\ \ t_0 + Tm]$.

3 Non-identical oscillators: the general case

To make our investigation closer to the real world problems, one has to consider an ensemble of non-identical oscillators. We will discuss the following system of equations

$$x_i' = (S + \mu_i) - (\gamma + \zeta_i)x_i, \tag{20}$$

where $0 \leq x_i \leq 1 + \xi_i, i = 1, 2, \ldots, n$. The constants S and γ are the same as in the last section such that $\kappa = \frac{S}{\gamma} > 1$. Moreover, constants μ_i and ζ_i are sufficiently small satisfying $\kappa_i = \frac{S + \mu_i}{\gamma + \zeta_i} > 1$. When $x_j(t) = 1 + \xi_j$, the oscillator fires and $x_j(t+) = 0$. The firing changes values of other oscillators $x_i, i \neq j$, such that

$$x_i(t+) = 0, \quad \text{if} \quad x_i(t) \geq 1 - \varepsilon \tag{21}$$

and

$$x_i(t+\tau+) = \begin{cases} x_i(t+\tau)+\varepsilon, & \text{if} \quad x_i(t+\tau) < 1-\varepsilon, \\ 0, \text{ otherwise}, \end{cases} \tag{22}$$

otherwise.

In what follows, we call real numbers $\varepsilon, \mu_i, \zeta_i, \xi_i, \varepsilon_i$, *parameters*, assuming the first one is positive. Moreover, constants $\mu_i, \zeta_i, \xi_i, \varepsilon_i$ will be called *parameters of perturbation*. To achieve the model of *identical oscillators*, assume that the parameters are all zero. In our case, an exhibitory model is under discussion, that is $\varepsilon + \varepsilon_i > 0$ for all i. Coupling is all-to-all such that each firing elicits jumps in all non-firing oscillators. If several oscillators fire simultaneously, then other oscillators react as just one oscillator fires. In other words, any firing acts only as a signal which abruptly provokes a state change, the intensity of the signal is not important, and pulse strengths are not additive. Moreover, we have that

$$x_i(s) = x_i(t)\mathrm{e}^{-(\gamma+\zeta_i)(s-t)} + \int_t^s \mathrm{e}^{-(\gamma+\zeta_i)(s-u)}(S+\mu_i)du,$$

near t.

Under the circumstances that condition (5) is valid, and constants μ_i and ζ_i are sufficiently small such that

$$\frac{\kappa_i - 1}{\kappa_i - 1 + \varepsilon} < \mathrm{e}^{-(\gamma+\zeta_i)\tau}, \tag{23}$$

we have $x_i(s) < 1$ for all $s \in [t, t+\tau]$, provided that $x(t) < 1-\varepsilon$.

We begin the present section by analyzing a couple of oscillators of the ensemble of n oscillators, and find that the couple synchronizes if parameters close to zero. After this, synchronization of the ensemble will be proved.

Consider the model of n non-identical oscillators given by relations (1) and (3). Fix two of them, let us say, x_l and x_r.

Lemma 2. *Assume that the inequalities (5), (7), (12), (14) and (19) are valid and* $t_0 \geq 0$ *is a firing moment such that* $x_l(t_0) = 1+\xi_i, x_l(t_0+) = 0$. *If parameters are sufficiently close to zero and absolute values of parameters of perturbation are sufficiently small with respect to* ε, *then the couple* x_l, x_r *synchronizes within the time interval* $[t_0, t_0+T]$ *if* $x_r(t_0+) \notin [a_0, a_1)$ *and within the time interval* $[t_0 + \frac{m-1}{2}\tilde{T}, t_0 + (m+1)T]$, *if* $x_r(t_0+) \in S_m, m \geq 1$.

Proof. If $1+\xi_r - \varepsilon - \varepsilon_r \leq x_r(t_0) \leq 1+\xi_r$, then two oscillators fire simultaneously, and we have only to prove the persistence of the synchrony, that will be discussed later. So, fix another oscillator $x_r(t)$ such that $0 \leq x_r(t_0) < 1+\xi_r - \varepsilon - \varepsilon_r$. If the couple is not synchronized, then there is a sequence $\{t_i\}$ of firing moments such that $0 \leq t_0 < t_2 < \ldots$, and the oscillator x_l fires at t_i, with i even, and x_r fires at t_i with odd i. For the sake of brevity let us notate $u_i = x_l(t_i), i = 2j+1$ and $u_i = x_r(t_i), i = 2j, j \geq 0$. In what follows we shall show that how one can evaluate u_{i+1} through $L(u_i)$. Consider the case i is even. There are $k \leq n-2$ distinct firing moments of the motion $x(t)$ in the interval (t_i, t_{i+1}). Denote by $t_i < \theta_1 < \theta_2 < \ldots < \theta_k < t_{i+1}$, the moments of firing, when at least one of the coordinates of $x(t)$ fires. We have that

$$\begin{aligned} x_r(\theta_1+\tau) &= (x_r(t_i+\tau)+\varepsilon+\varepsilon_r)\mathrm{e}^{-(\gamma+\zeta_r)(\theta_1+\tau-t_i)} + \kappa_r(1-\mathrm{e}^{-(\gamma+\zeta_r)(\theta_1+\tau-t_i)}), \\ x_r(\theta_2+\tau) &= (x_r(\theta_1+\tau)+\varepsilon+\varepsilon_r)\mathrm{e}^{-(\gamma+\zeta_r)(\theta_2-\theta_1)} + \kappa_r(1-\mathrm{e}^{-(\gamma+\zeta_r)(\theta_2-\theta_1)}), \\ &\ldots\ldots \\ x_r(\theta_j+\tau) &= (x_r(\theta_{j-1}+\tau)+\varepsilon+\varepsilon_r)\mathrm{e}^{-(\gamma+\zeta_r)(\theta_j-\theta_{j-1})} + \kappa_r(1-\mathrm{e}^{-(\gamma+\zeta_r)(\theta_j-\theta_{j-1})}), \\ &\ldots\ldots \\ x_r(t_{i+1}) &= (x_r(\theta_k+\tau)+\varepsilon+\varepsilon_r)\mathrm{e}^{-(\gamma+\zeta_r)(t_{i+1}-\theta_k-\tau)} + \kappa_r(1-\mathrm{e}^{-(\gamma+\zeta_r)(t_{i+1}-\theta_k-\tau)}). \end{aligned} \tag{24}$$

The moment t_{i+1} satisfies the following

$$1+\xi_r-\varepsilon-\varepsilon_r \le x_r(t_{i+1}) \le 1+\xi_r, \tag{25}$$

and continuously depends on parameters and $x_r(t_i)$.

We have also that

$$\begin{aligned}
x_l(\theta_1+\tau) =& \ \kappa_l(1-\mathrm{e}^{-(\gamma+\zeta_l)(\theta_1+\tau-t_i)}),\\
x_l(\theta_2+\tau) =& \ (x_l(\theta_1+\tau)+\varepsilon+\varepsilon_l)\mathrm{e}^{-\gamma(\gamma+\zeta_l)(\theta_2-\theta_1)}+\kappa_l(1-\mathrm{e}^{-(\gamma+\zeta_l)(\theta_2-\theta_1)}),\\
& \ \cdots\cdots\\
x_l(\theta_j+\tau) =& \ (x_l(\theta_{j-1}+\tau)+\varepsilon+\varepsilon_l)\mathrm{e}^{-(\gamma+\zeta_l)(\theta_j-\theta_{j-1})}+\kappa_l(1-\mathrm{e}^{-(\gamma+\zeta_l)(\theta_j-\theta_{j-1})}),\\
& \ \cdots\cdots\\
x_l(t_{i+1}) =& \ (x_l(\theta_k+\tau)+\varepsilon+\varepsilon_l)\mathrm{e}^{-(\gamma+\zeta_l)(t_{i+1}-\theta_k-\tau)}+\kappa_l(1-\mathrm{e}^{-(\gamma+\zeta_l)(t_{i+1}-\theta_k-\tau)}).
\end{aligned} \tag{26}$$

The last two formulas describe the dependence of u_{i+1} on u_i. One can easily find a similar relation for the case i is odd.

Set $\delta_i(\mu_i,\zeta_i)=\kappa_i-\kappa$. It is clear that $\delta_i(0,0)=0$. By means of (24) and (26), it is possible to achieve that

$$\begin{aligned}
x_r(t_{i+1}) =& \ (x_r(t_i+\tau)+\varepsilon)\mathrm{e}^{-\gamma(t_{i+1}-t_i)}\mathrm{e}^{-\zeta_r(t_{i+1}-t_i)}\\
&+\kappa(1-\mathrm{e}^{-(\gamma+\zeta_r)(t_{i+1}-t_i)})\\
&+\varepsilon_r\mathrm{e}^{-\gamma(t_{i+1}-t_i)}\mathrm{e}^{-\zeta_r(t_{i+1}-t_i)}\\
&+(\varepsilon+\varepsilon_r)\sum_{j=1}^{k}\mathrm{e}^{-(\gamma+\zeta_r)(t_{i+1}-\theta_j-\tau)}\\
&+\delta_r(1-\mathrm{e}^{-(\gamma+\zeta_r)(t_{i+1}-t_i)}),
\end{aligned} \tag{27}$$

and

$$x_l(t_{i+1})=(\kappa+\delta_l)(1-\mathrm{e}^{-(\gamma+\zeta_l)(t_{i+1}-t_i)})+(\varepsilon+\varepsilon_l)\sum_{j=1}^{k}\mathrm{e}^{-(\gamma+\zeta_l)(t_{i+1}-\theta_j-\tau)}. \tag{28}$$

Now, recall the map L_D defined in the last section. One can find out that

$$\phi(\bar{t}_{i+1})=(x_r(t_i+\tau)+\varepsilon)\mathrm{e}^{-\gamma(\bar{t}_{i+1}-t_i-\tau)}+\kappa(1-\mathrm{e}^{-\gamma(\bar{t}_{i+1}-t_i)}), \tag{29}$$

where $\bar{t}_{i+1}$ satisfies

$$\phi(\bar{t}_{i+1})=1, \tag{30}$$

and

$$\psi(\bar{t}_{i+1})=\kappa(1-\mathrm{e}^{-\gamma(\bar{t}_{i+1}-t_i)}). \tag{31}$$

By the help of the definition of L_D, we attain that $L_D(u_i)=\psi(\bar{t}_{i+1})$.

Without loss of generality assume that $\bar{t}_{i+1}\le t_{i+1}$. In this case, one has

$$\phi(\bar{t}_{i+1})-x_r(\bar{t}_{i+1})=1-x_r(\bar{t}_{i+1})=\Phi_1(\varepsilon,\varepsilon_r,\zeta_r,\delta_r,\tau), \tag{32}$$

where

$$\begin{aligned}
\Phi_1(\varepsilon,\varepsilon_r,\zeta_r,\delta_r,\tau) =& \ \kappa(1-\mathrm{e}^{-\gamma(\bar{t}_{i+1}-t_i)})(\mathrm{e}^{-\zeta_r(\bar{t}_{i+1}-t_i)}-1)\\
&-(x_r(t_i+\tau)+\varepsilon)\mathrm{e}^{-\gamma(\bar{t}_{i+1}-t_i)}(\mathrm{e}^{-\zeta_r(\bar{t}_{i+1}-t_i)}-1)\\
&-\varepsilon_r\mathrm{e}^{-\gamma(\bar{t}_{i+1}-t_i)}\mathrm{e}^{-\zeta_r(\bar{t}_{i+1}-t_i)}-(\varepsilon+\varepsilon_r)\sum_{j=1}^{k}\mathrm{e}^{-(\gamma+\zeta_r)(\bar{t}_{i+1}-\theta_j-\tau)}\\
&-\delta_r(1-\mathrm{e}^{-(\gamma+\zeta_r)(\bar{t}_{i+1}-t_i)}),
\end{aligned}$$

and the last expression tends to zero as all of its arguments tend to zero. Next, by utilizing (25) and (32) we achieve that $t_{i+1} - \overline{t_{i+1}} \leq \Phi_2(\varepsilon, \varepsilon_r, \zeta_r, \delta_r)$, where

$$\Phi_2(\varepsilon, \varepsilon_r, \zeta_r, \delta_r, \tau) \equiv \frac{|\xi_r| + \varepsilon + |\varepsilon_r| + \Phi_1(\varepsilon, \varepsilon_r, \zeta_r, \delta_r, \tau)}{S - |\mu_r| - \gamma - |\zeta_r|}.$$

Now, by means of the last equation, (28) and (31), one can see that

$$\begin{aligned} |L_D(u_i) - K_i(u_i)| = & \ |x_l(t_{i+1}) - \psi(\overline{t_{i+1}})| \leq |x_l(t_{i+1}) - x_l(\overline{t_{i+1}})| \\ & + |x_l(\overline{t_{i+1}}) - \psi(\overline{t_{i+1}})| \\ \leq & \ \Phi_2(S + |\mu_l| + \gamma + |\zeta_l|) + \Phi_1. \end{aligned}$$

That is, difference $L_D(u_i, \varepsilon) - u_{i+1}$ can be made arbitrarily small if the parameters are sufficiently close to zero. Moreover, we should assume smallness of absolute values of the parameters of perturbation with respect to ε, to satisfy (25). This convergence is uniform with respect to u_0. We can also vary the number of points θ_i and their location in the intervals (t_j, t_{j+1}) between 0 and $n-1$. The convergence is indifferent with respect to these variations, too.

Consider $L_D^i(u_0, \varepsilon)$. It is true that $L_D^m(u_0, \varepsilon) \in [1 - \varepsilon, 1]$. Assume, without lost of generality, that m is an even number. Since L_D is a continuous function, we can find recurrently, by applying the following sequence of inequalities $|u_i - L_D^i(u_0, \varepsilon)| \leq |u_i - L_D(u_{i-1}, \varepsilon)| + |L_D(u_{i-1}, \varepsilon) - L_D(L_D^{i-1}(u_0, \varepsilon))|, i = 1, 2, \ldots,$ that either $1 + \xi_r - \varepsilon - \varepsilon_r < u_m < 1 + \xi_r$ or $1 + \xi_l - \varepsilon - \varepsilon_l < u_{m+1} < 1 + \xi_l$, if the parameters are sufficiently small. From the notation it implies that each of the last two inequalities bring the couple to synchronization. Similarly, one can discuss relations connected to inequality (19).

Since each of the iterations of L_D is done within interval with length not more than T, we obtain now that the couple x_l, x_r is synchronized not later than $t = t_0 + (m+1)T$.

We have found that oscillators x_l and x_r fire in unison at some moment $t = \theta$. Next, we show that they will save the state, being different. To find conditions for this, let us denote by $\tau > \theta$ the next moment of firing of the couple. Let say, x_r fires at this moment. Thus, we have that $x_l(\theta+) = x_r(\theta+) = 0$. Then $x_l(t) = x_r(t), \theta \leq t \leq \tau$. It is clear that to satisfy $x_l(\tau+) = x_r(\tau+) = 0$, we need $1 + \xi_r - \varepsilon - \varepsilon_r \leq x_l(\tau)$. By applying formula (25) again, this time with $t_i = \theta, t_{i+1} = \tau$, one can easily obtain that the inequality is correct if parameters are close to zero and absolute values of the parameters of perturbation are small with respect to ε. Thus, one can conclude that if a couple of oscillators is synchronized at some moment of time than it continues to fire in unison for ever. The lemma is proved.□

Let us extend the result of the last Lemma for the whole ensemble.

Theorem 3. *Assume that the conditions (5), (7), (12), (14) and (19) are valid, and $t_0 \geq 0$ is a firing moment such that $x_j(t_0) = 1 + \xi_j, x_j(t_0+) = 0$. If the parameters are sufficiently close to zero, and absolute values of parameters of the perturbation are sufficiently small with respect to ε, then the motion $x(t)$ of the system synchronizes within the time interval $[t_0, t_0 + T]$, if $x_i(t_0+) \notin [a_0, a_1), i \neq j$, and within the time interval $[t_0 + \frac{\max_{i \neq j} k_i - 1}{2} \tilde{T}, t_0 + (\max_{i \neq j} k_i + 1)T]$, if there exist $x_s(t_0+) \in [a_0, a_1)$, for some $s \neq j$ and $x_i(t_0+) \in S_{k_i}, i \neq j$.*

Proof. Consider the collection of couples $(x_i, x_j), i \neq j$. Each of these pairs synchronizes by the last Lemma within interval $[t_0 + \frac{\max_{i \neq j} k_i - 1}{2} \tilde{T}, t_0 + (\max_{i \neq j} k_i + 1)T]$. The theorem is proved.

Let us introduce a more general system of oscillators such that Theorem 3 is still true.

Consider a system of n oscillators given such that if $i-$th oscillator does not fire or jump up, it satisfies $i-$th equation of system (1). If several oscillators $x_{i_s}, s = 1, 2, \ldots, k$, fire such that $x_{i_s}(t) = 1 + \phi(t, x(t), x(t - \tau_{i_s}))$, where $|\phi(t, x(t), x(t - \tau_i))| < \xi_i, i = 1, 2, \ldots, n$, and $x_{i_s}(t+) = 0$, then all other oscillators $x_{i_p}, p = k+1, k+1, \ldots, n$, change their coordinates by law

$$x_i(t+) = 0, \text{ if } x_i(t) \geq 1 - \varepsilon \tag{33}$$

and, if $x_i(t) < 1-\varepsilon$, then

$$x_i(t+\tau+) = x_i(t+\tau)+\varepsilon+\sum_{s=1}^{k}\varepsilon_{i_p i_s}. \tag{34}$$

One can easily see that the last theorem is correct for the model just have been described, if $\varepsilon+\sum_{s=1}^{k}\varepsilon_{i_p i_s} > 0$, for all possible k, i_p and i_s, and we assume that ε_{ij} are also parameters of perturbation. Moreover, one can easily see that initial functions for thresholds conditions can be chosen arbitrarily with values in the domain of the system.

Remark 1. Our preliminary analysis shows that the dynamics in a neighborhood of v^* can be very complex. We do not exclude that a chaos appearance can be observed, and trajectories may belong to a fractal, if parameters are not small. It does not contradict to the zero Lebesgue measure of non-synchronized points. Possibly, analysis of non-identical oscillators with not small parameters is of significant interests to explore arrhythmias, earthquakes, chaotic flashing of fireflies, etc.

Remark 2. The time of synchronization for a given initial point does not increase if the number of oscillators increases (but the parameters needed to be closer to zero). This property, possibly, can be accepted as a small-world phenomenon.

4 The simulation result

To demonstrate our main result numerically, let us consider a model of 100 oscillators, which initial values are randomly uniform distributed in $[0,1]$. Their differential equations are of form

$$x_i' = (4.1+0.01*sort(rand(1,n)) - (3.2+0.01*sort(rand(1,n))x_i,$$

and thresholds

$$1+0.005*sort(rand(1,n)), i = 1,2,\ldots,100,$$

where deviations of coefficients the threshold are also uniformly random in $[0,1]$. We place the result of simulation with $\varepsilon = 0.06$ and $\tau = 0.002$ in Figure 3, where the state of the system is shown at the initial moment, before the 183−th jump, before the 366−th jump and the last is before the 549−th jump. That is, it is obvious that eventually all oscillators fire in unison.

We verified that all conditions (5),(7),(12),(14) and (19) are valid.

5 Conclusion

The cardiac pacemaker model of identical and non-identical oscillators with delayed pulse-couplings is investigated in the paper. We apply the method developed in [13]- [14], which is based on a specially defined map. Sufficient conditions are found such that involvement of delay in the Peskin's model does not change the synchronization result for identical and non-identical oscillators [2,3,13]. What we have done admits a biological sense, since retardation is often presents in biological processes and if one proves that a phenomenon preserves even with delays, that makes us more confident that the model is adequate to the reality. Moreover, the method of treatment of models with delay can be useful for neural networks and earthquake faults [5,6,32–34] analysis. All the proved assertions are true with $\tau = 0$. Indeed, it is easy to see that conditions (5), (7), (12), (14) and (19) are valid with $\tau = 0$. Thus, the synchronization results for the Peskin's model in [13,14] are confirmed one more time. In next our papers we suppose to give analysis for models with non-small delays. There are several interesting problems, which can develop results of the present paper further. Let us name some of them. Suppose that condition (19) is violated. That is, $\tilde{v} > a_2$. Consider two identical oscillators. The corresponding graph of

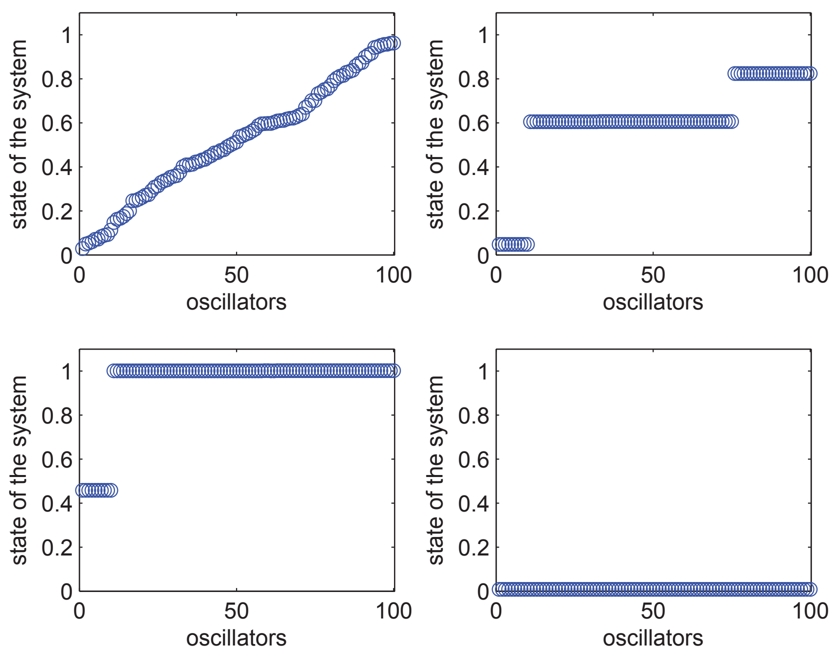

Fig. 3 The state of the model before the first, the 183−th, 366−th, and 549−th jump is seen. The flat fragments of the graph are groups of oscillators firing in unison.

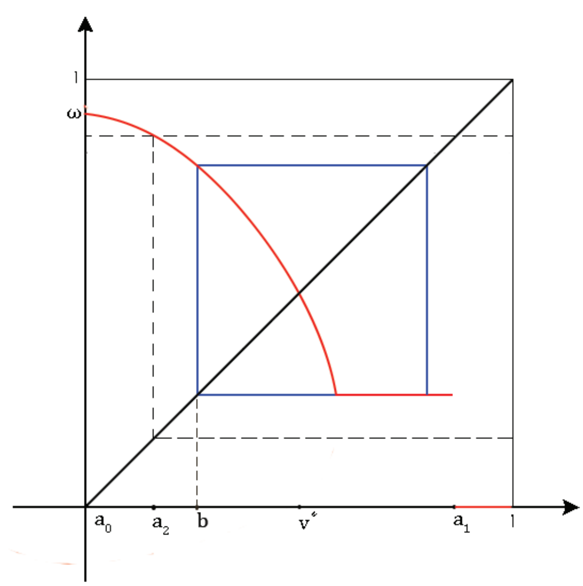

Fig. 4 It is seen that the couple synchronizes after not more than three iterations, if $v \notin [b, a_1]$. Otherwise the pair moves periodically with period 2 ultimately.

the map looks as in Figure 4. One can see from the picture that the couple synchronizes after not more than three iterations, if $v \notin [b, a_1]$. Otherwise the pair moves periodically with period 2 ultimately. Considering this simple case of two identical oscillators, one can predict that for an ensemble of oscillators (identical or not quite identical) there should be two or more clusters of synchronized oscillators, and the clusters may move periodically, if $\tilde{v}$ is near a_2. In our simulations, we observe clustering as well as periodicity in the motion of the clusters. Since the number of clusters changes with the variation of the parameters, one can investigate bifurcation of periodic solutions as well as the number of clusters.

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