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ANALYSIS OF MUTUAL SYNCHRONIZATION OF COUPLED SELF-OSCILLATING BIOLOGICAL SYSTEMS

Губаль Г. М. Аналіз взаємної синхронізації зв'язаних автоколивальних біологічних систем. У статті досліджено зв'язані автоколивальні біологічні системи і проаналізовано їхню взаємну синхронізацію. Наведено приклади таких систем.
Ключові слова: синхронізація, автоколивальна система, клітина, біологічна система.
Літ. 3.
Губаль Г. Н. Анализ взаимной синхронизации связанных автоколебательных биологических систем. В статье исследовано связанные автоколебательные биологические системы и проанализировано их взаимную синхронизацию. Приведены примеры таких систем. .
Ключевые слова: синхронизация, автоколебательная система, клетка, биологическая система.
Лит. 3.
Hubal H. M. Analysis of mutual synchronization of coupled self-oscillating biological systems. In the article, coupled self-oscillating biological systems are studied and their mutual synchronization is analyzed. Examples of such systems are given.
Keywords: synchronization, self-oscillating system, cell, biological system.
Bibl. 3.

Introduction. There are auto-oscillations and the mutual synchronization of these oscillations in the life of individual cells and cell groups. Various cell organelles such that the nucleus, ribosomes, mitochondria oscillate changing their shape and volume [1-3].

For example, periodic changes in the size of cell nuclei (oscillations of cell nuclei) were observed in the suspension of ascid cell carcinoma of Ehrlich (a special type of cancer cells). The period of reproduction, that is the time from one division to the other for this type of cells is about one day. During the life of these cells, their nuclei have time to shrink, and then swell 25-30 times.

Oscillations of cell nuclei promotes a more intense metabolism between the nucleus and the cytoplasm of the cell, in particular the more intense exchange of molecules that carry genetic information. Since there was a periodic change in the average size of nuclei, and averaging was performed on many thousands of cells, it can be argued that the oscillations of the nuclei in these cells are synchronized, that is, there is a mutual synchronization. Otherwise, on average, no periodic change in size would have been observed.

Main part. Consider synchronization of oscillations in biological systems.

Two periodic processes will be synchronous if their frequencies are equal or multiple to one another, and the phase shift over time stays constant.

Let in the case of synchronous harmonic oscillations in the antiphase we have oscillations:

$$x_1(t) = a\sin\omega t, \quad x_2(t) = a\sin(\omega t - \pi) = -a\sin\omega t.$$

Then the sum of these oscillations has the form

$$x(t) = x_1(t) + x_2(t) = 0.$$

In the case of synchronous sinusoidal oscillations with zero phase difference

$$x_1(t) = a\sin\omega t, \quad x_2(t) = a\sin\omega t,$$

we have the sum of these oscillations

$$x(t) = x_1(t) + x_2(t) = 2a\sin\omega t.$$

As we can see, in this case, the amplitude of the total oscillation doubles.

If we sum up two non-synchronous processes which are described, for example, by equations

$$x_1(t) = a\cos\omega_1 t, \quad x_2(t) = a\cos\omega_2 t$$

with slightly different frequencies (that is

$$|\omega_1 - \omega_2| \ll \omega_1 \approx \omega_2), \qquad (1)$$

then the total oscillation

$$x(t) = x_1(t) + x_2(t) = a\cos\omega_1 t + a\cos\omega_2 t,$$

in this case, has the beat shape (Fig. 1). Let us show it.

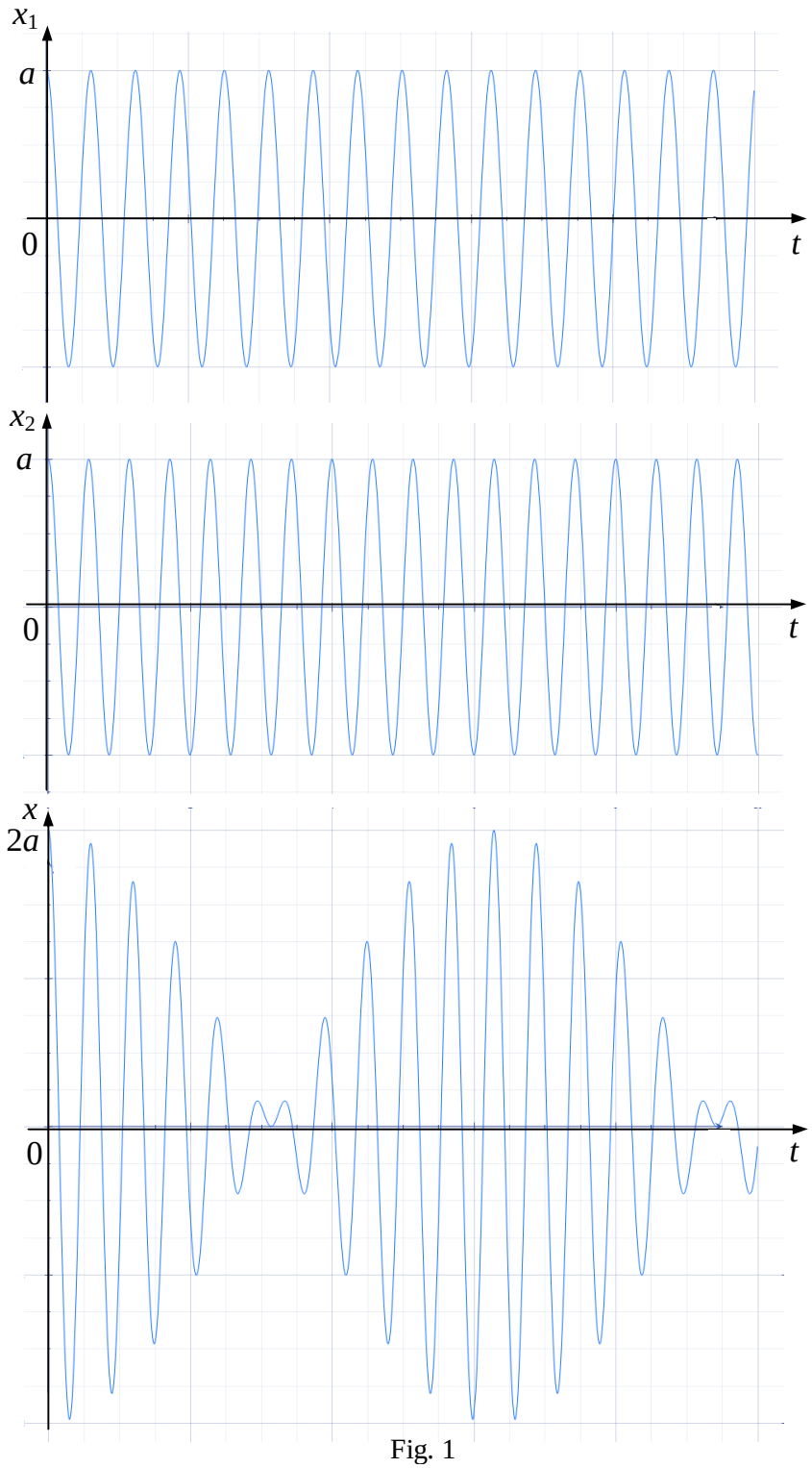

Fig. 1

The sum of these oscillations has the form

$$x(t) = x_1(t) + x_2(t) = a(\cos\omega_1 t + \cos\omega_2 t) = 2a\cos\frac{\omega_1 + \omega_2}{2}t\cos\frac{\omega_1 - \omega_2}{2}t.$$

We denote the value $\frac{\omega_1 + \omega_2}{2}$ by ω, and the value $\frac{\omega_1 - \omega_2}{2}$ by Ω. Then we obtain the total oscillation

$$x(t) = 2a\cos\omega t\cos\Omega t = X_1(t)X_2(t), \qquad (2)$$

where

$$X_1(t) = \cos\omega t = \cos\frac{2\pi}{\tau}t, \quad X_2(t) = 2a\cos\Omega t = 2a\cos\frac{2\pi}{T}t,$$

$\tau = \frac{2\pi}{\omega}$ is the period of oscillations, and $T = \frac{2\pi}{\Omega}$ is the beat period.

Note, taking into account inequality (1), we can assume that

$$\frac{\omega_1 + \omega_2}{2} = \omega \approx \omega_1 \approx \omega_2, \quad \frac{\omega_1 - \omega_2}{2} = \Omega \ll \omega.$$

The obtained expression (2) determines the shape $x(t)$ in the form of beat (Fig. 2). We put $a = 1$ in figures.

As we can see, the graphs of the function $x(t)$ are the same in Fig. 1 and Fig. 2. The graph of the function $x(t)$ is obtained by means of the sum $x_1(t) + x_2(t) = x(t)$ in Fig.1, and by means of the product $X_1(t)X_2(t) = x(t)$ in Fig. 2.

If we form the sum of *n* synchronous oscillations with the frequency ω and with zero phase shift, then we obtain oscillations with the same frequency. In this case, the amplitude of the total oscillation is greater than the amplitude of the summands *n* times. We will not get anything like this if we add *n* non-synchronous oscillating processes with similar frequencies. If the sum of two non-synchronous oscillations with close frequencies has the correct beat shape, then the sum of *n* such oscillations will already have the form of a rather complex curve.

Self-oscillating systems are capable of automatic mutual synchronization if they are interconnected. So, if you connect the self-oscillating systems to one system, then you do not have to think about special devices that will provide synchronization, - it arises itself.

The self-oscillating system is described by a stable boundary cycle and its amplitude is stable with respect to deviations away from the boundary cycle. However, if a point, as a result of any third-party action, jumps forward or back along the boundary cycle, then no force will return it to the previous place. Self-oscillating systems are not stable with respect to changes in the phase of oscillations. Therefore, even identical, non-interconnected self-oscillating systems, first, oscillate in one phase, synchronously, under the action of random jerks, will change the phase of oscillations in time, and, thus, the sum of their oscillations will be an oscillating process with random beat. If there is a sufficient connection between self-oscillating systems (in the case of chemical oscillators, the exchange of substances by means of diffusion), then self-oscillations in these systems become synchronous, even if the frequencies of oscillations in these systems do not differ significantly from one another.

One example of synchronous oscillations in biological systems is the work of the heart.

The work of the heart is one of the most perfect self-oscillating systems created by nature. Correctness of the work of the heart is determined by the synchronous work of entire groups of muscles, which provide alternating contraction of the ventricles and atria. The synchronization of this work is provided by a sinus node which produces with a certain frequency synchronizing pulses of electrical voltage. If the synchronous mode of heart muscle contraction is violated, then the so-called fibrillation may occur that are chaotic cramps of individual fibers of the heart muscle, which, if not applied to emergency measures, lead to the death of the body. Urgent measures consist in violent synchronization of the heart by means of special massage or by means of electrical impulses from the laboratory generator. Sometimes a miniature electronic synchronizing pulse generator is even implanted in the body. The synchronization of the oscillations of the heart muscle passes at the physiological level, in which the nervous system plays a major role.

If the cells with oscillating nuclei are bound in any way with each other, then the oscillations in each of the cells must be synchronized.

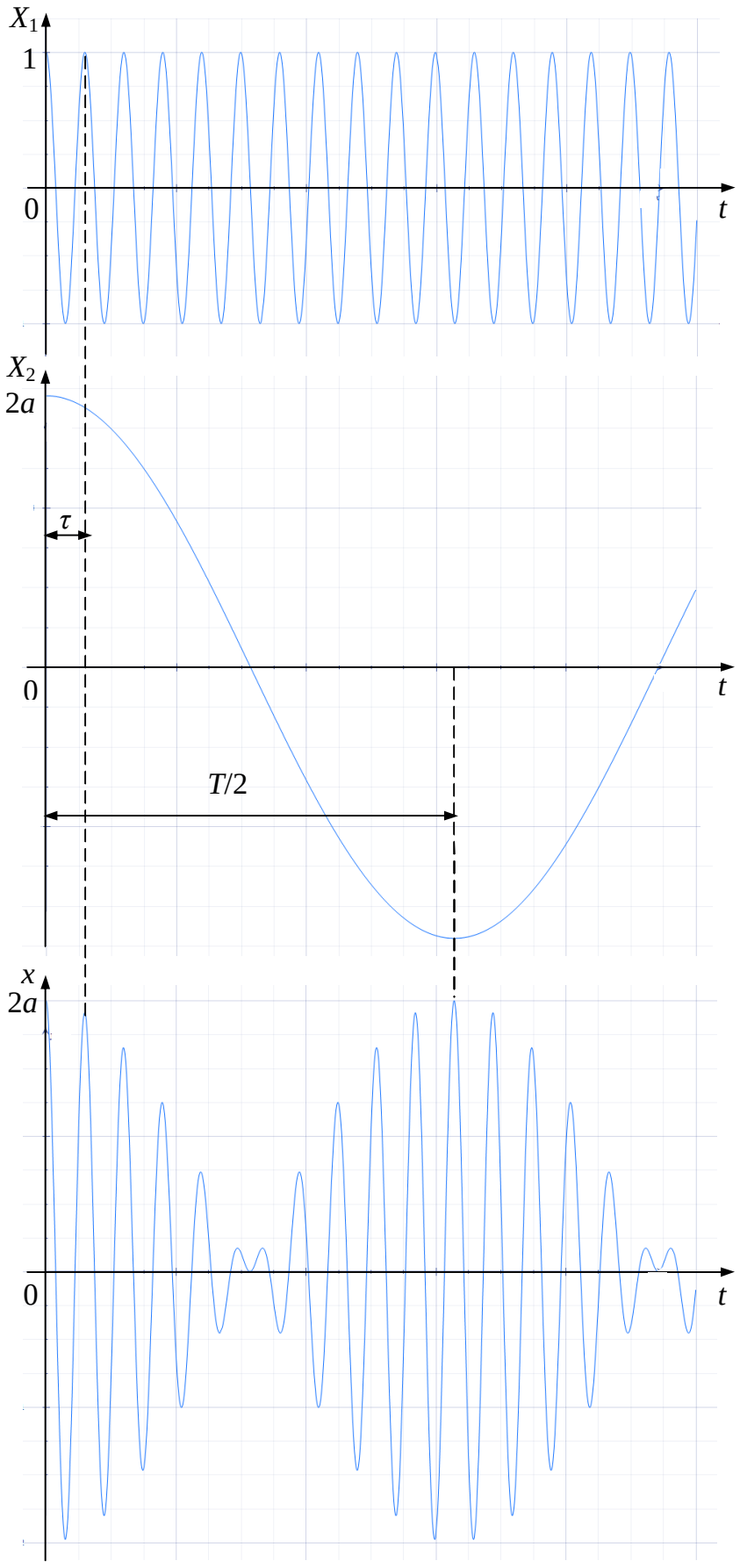

Fig.2

Let the cells be located in some volume *V* in suspense in the physiological solution (Fig.3, metabolism between cells and the environment is depicted by arrows).

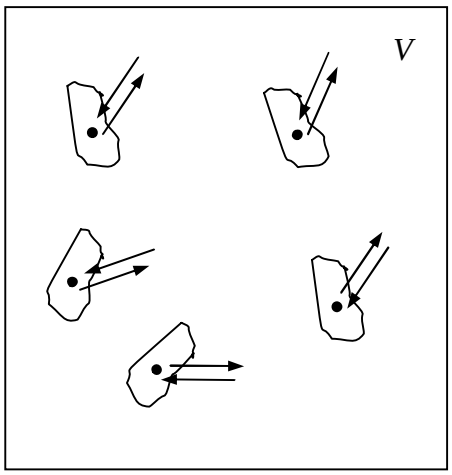

Fig. 3

Assuming that the nuclei periodically emit active substances in the cytoplasm, it can also be assumed that some of these active substances or products formed under the action of these substances penetrate through the cell membranes into the liquid in which the cells float. We denote these products with the letter *P*, and the active substances with the letter *S*. You can, for example, present such a mechanism of pulsation of the nucleus. The nucleus swells under the pressure of the substances *S* produced therein, and this swelling continues until there are enough products *P* in the cytoplasm (off-nucleous content) of the cell. If these products are used or diffused through the membranes of the cells outside, then the nucleus is shrunk, the cytoplasm is enriched with the active substance *S*, the presence of which leads to the formation of products *P*.

Thus, the scheme of regulation of oscillations may look as follows: the product *P* allows the swelling of the nucleus. If it is less than a certain threshold, then the nucleus shrinks and releases the active substance *S*, which leads to the formation of *P*, etc.

We now turn to the mutual synchronization of the oscillations of nuclei in separate cells. According to our assumption, the molecules of *P* fall into the intercellular environment. Assuming that they may partially fall into the middle of the cell from the outside, then it may turn out that the excess of the molecules of *P* that came from one cell falls into the middle of the neighbouring cell and will delay the moment of the shrinkage of the nucleus in that neighbouring cell. On the other hand, if in the intercellular environment. the substance *P* was found to be inadequate, then it would diffuse more intensively from the cell where it is abundant. Therefore, the moment of the shrinkage of the nucleus can occur earlier.

It follows that if there is a variation in the number of molecules of the product *P* in one of the cells, it can cause a delay or acceleration of the shrinkage of the nucleus in the neighboring cells. And this is a necessary condition for the occurrence of synchronous oscillations of nuclei in neighboring cells.

First, let the oscillation of nuclei in cells be non-synchronous. Then, the total concentration of the substance *P* in the intercellular environment as a function of time will have the form of a complex curve. As more and more cells with synchronous oscillating nuclei become more in the suspension, the dependence of the concentration of the substance *P* on time in the intercellular environment becomes more and more similar to the correct periodic function, which means that mutual synchronization will be carried out more easily. Thus, here we have the case of many connected (parallel-connected) operating synchronous and in-phase generators, only they produce the substance *P* instead of the electricity, and the intercellular environment is the load for cell generators.

Consider, for example, the coexistence of rice and hares. The oscillation in the number of these animals is based on the collection of data from a large area, which is separated by rivers and other natural barriers to separate areas, the combination between which for animals may be in one way or another complicated.

Assume that these areas are completely isolated from each other. Then in each of these areas the number of rice and hares would change in a oscillating manner. However, the phases and frequencies of the oscillations in these isolated areas would be independent. Then there could not be observed noticeably periodic process throughout the territory in average, but there would be purely random deviations from some middle level. If we now assume that at some moment a part of the animals can flow from one area to another (diffuse through obstacles), then the process of mutual synchronization of oscillations will go. After some

time of establishment (from the beginning of the oscillation), the number of individuals will be synchronized in all its areas throughout the territory. Here we deal with the same general principle as in the case of the mutual synchronization of cell nucleus shrinkage. If oscillations can occur in separate parts of a complex system and there is a connection between these parts, then sooner or later the oscillations will become synchronous.

There are also oscillations in the size and shape of mitochondria and ribosomes in the cells. Synchronous oscillations of these organelles can take place at a much higher frequency than the oscillations of the nuclei, namely, with the frequency of order of ten oscillations per second. The mutual synchronization of these oscillations can be due to the connection through metabolites of the cytoplasm (i.e., through substances formed in the off-nucleus cell protoplasm as a result of metabolism). You can imagine and completely different ways of connection, for example, by means of acoustic or electromagnetic waves, which are emitted and absorbed by the oscillating molecules, from which these organelles are constructed.

The above-studied oscillating regime for living organisms gives:

- coordination in time of the course of various biochemical processes;
- the presence of the mechanism of "biological clock";
- all types of movements from the beats of cilia and flagella (which are the organs of movement of the simplest unicellular organisms), and the movement of the protoplasm (the content of the cell) to the rhythmic contraction of the heart and the work of transversely muscle;
- interaction of cells in the process of morphogenesis, that is the formation of tissues and organs in the developing organism;
- the main mechanism of the enzymes

Conclusions. Coupled self-oscillating biological systems are studied and their mutual synchronization is analyzed. Examples of such systems are given. It is shown It is shown what the studied oscillating regime gives for the existence of living organisms.

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