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Pharmacy and Drug Development
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ISSN: 2836-2322

RESEARCH ARTICLE

Development of methods for mathematical modeling of endothelium. In silico modeling of the structures of the cardiovascular system (CSS) based on a model from the theory of automatic control (TAU)

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Received: 09 September 2022; **Accepted:** 21 September 2022; **Published:** 31 October 2022.

Citation: Kanistov Vasil Lyubenov, (2022). Development of methods for mathematical modeling of endothelium. In silico modeling of the structures of the cardiovascular system (CSS) based on a model from the theory of automatic control (TAU). Journal of Pharmacy and Drug Development. 1(2). DOI: 10.58489/2836-2322/006

Abstract

On the basis of the model from the theory of automatic control (TAU) and the development of an adequate and effective mathematical model of the endothelium, to simulate in silico the structures of the cardiovascular system (CCC), as elements of the physico-biological system of automatic regulation (FBSAR). We introduce the mathematical model "nozzle-damper-bellows" - as a theoretical and experimental justification for the construction and development of a mathematical model: endotheliocyte, endothelium, smooth muscle cells (MMC) and the vessel wall. On this basis, we will draw up a structural and functional scheme of the physico-biological control object (FBOU), as a dynamic link in the composition of the physico-biological system of automatic regulation (FBSAR). The conclusions of the mathematical model have been reformulated and the in-silico modeling of the structures of the cardiovascular system (CCC) based on the model from the theory of automatic control (TAU), gives us the possibility of adapted processes into automatic control systems (CAP) on processes in physico-biological automatic control systems (FBSAR). Based on the automatic control system (CAP) of the physical process, structured from the regulator (**R**) and the control object (**OC)** (Figure 4), we have created a physico-biological automatic control system (FBSAR) and the corresponding physico-biological control objects (FBOU). The tuning coefficients introduced by the mathematical model of the control object (OC) and the regulator (R) in automatic control systems (CAP) are similar to the tuning coefficients of homeostasis for real physical and biological control objects (FBOU), and physico-biological automatic control systems (FBSAR). The main effects on the pharmacological target of the cardiovascular system, like physico-biological automatic control systems (FBSAR) are the coefficients of adjustment of practical implemented connections in automatic control systems (ATS), from the theory of automatic control (TAU). Research processes of homeostasis of the cardiovascular system **(CCC)** in fundamental pharmacology and medicine. The application of in silico modeling of the structures of the cardiovascular system (CCC) based on the model from the theory of automatic control (TAU) to the research processes of fundamental pharmacology and medicine can be done (necessarily) under the supervision of interdisciplinary specialists.

Keywords: *mathematical modeling, in silico structures, endothelium, endothelial cell, smooth muscle cells (MMC), vessel wall, cardiovascular system (CCC), physico-biological control objects (FBSAR), physico-biological systems of automatic regulation (FBSAR)*

Introduction

Over the past 30-35 years, the efforts of researchers have been aimed at creating and applying methodological approaches to assessing the function of the cardiovascular system and its most important links, like the endothelial system [1].

For the study of the pharmacological properties of drugs used to treat the cardiovascular system (CCC), it is critically important, the choice of experimental models turned out to be successful. Subsequently, studies of the direction and effectiveness of potential drugs for the treatment of disorders of the functional state of the cardiovascular system (CVS) depend on this model.

Although rare, in scientific theory and practice, the most successful models have been created in the community of specialists – mathematicians, physicists, engineers – on the one hand, and doctors, pharmacologists and biologists on the other. All these specialists have interdisciplinary knowledge, know well and work with any modeling objects. In the process of joint work of specialists, the most difficult part is the formalization of knowledge about the object and the physiological processes in it, in a language that can then be reformulated into a physical, and then into a mathematical (usually dynamic model) and / or an in-silico model of structures acting on pharmacological targets of the cardiovascular system.

But the more challenging part of these processes is the way back – extrapolating the data obtained from biological models to humans.

We consider the cardiovascular system (CCC) as a closed system of organs that ensures blood circulation in the body.

The composition of the cardiovascular system includes the heart and blood vessels. The endothelium together with the vascular wall is a single organ of the circulatory system with the corresponding specific functions. The endothelium, together with the vascular wall of the artery and vein, is an integral (holistic) organ, "is able to respond to mechanical action (for example, cyclic stretching or fluid shift tension): leaking blood, the amount of blood pressure in the lumen of the vessel and the degree of tension of the muscular layer of the vessel" [2].

All this constitutes the objects of control (OU) and control that we subject to scientific research methodologies - Physical and Biological Control Objects (FBOU)

The physical and biological functions of the cardiovascular system (CCC) are skillfully coordinated due to neuro-reflex regulation (R), which makes it possible to maintain homeostasis in physico-biological control objects (FBOU) under constantly changing conditions of the external and internal environments.

After applying the reformulated conclusions to the mathematical model and in silico modeling of the structures of the cardiovascular system (CCC) based on the model from the theory of automatic control (TAU), we are given the opportunity to apply processes in automatic control systems (CAP) to physico-biological automatic control systems (FBSAR). Which systems are usually composed of control object (OC) and regulator (R). (Figure 4)

The last part of the modeling processes – the application of pharmacological results in mathematical models in biological systems like FBOU and FBSAR, practically remains partially implemented!

In automatic control theory (TAU), functional structural diagrams are a numerical and graphical interpretation of a mathematical model of an automatic control system (CAP). The elements that build structural systems are called links. Each link is usually represented and designated with its own transfer function - that is, its mathematical model.

The requirement for the structure of physico-biological systems is to obtain the transfer function of the system (in the form of:) and, by equating the denominator, leads to the obtaining of the so-called. a characteristic equation of an automatic control system (CAP) or its mathematical model.

Materials and Methods

A. Mathematical model "nozzle-damper-bellows" - as a theoretical and experimental justification for the construction and development of a mathematical model: endotheliocyte, endothelium, smooth muscle cells (MMC) and the vessel wall.

The physical model of the bellows corresponds to the biological model of the closed vascular system of a person (cardiovascular system of the CCC) is represented from blood vessels - hollow tubes through which blood moves.

The reactions of the endothelium and smooth muscle cells (MMC) vessel wall to mechanical and chemical influences lead us to the application of the pneumatic-mechanical model [3]. The model represented by the type of "nozzle-damper-bellows" (Figure 2) - physico-biological objects of control (FBOU) endothelium and smooth muscle cells (MMC) vessel wall, and corresponding to this model, a mathematical model in the form of a transfer function ().

Endothelial cells, in addition to mechanical influences, are sensitive to chemical influences.

The reaction of the endothelium, or rather endothelial cells - endothelial cells, to mechanical effects and chemical effects are at least conditionally equivalent, and leads to synthesis and isolation on the so-called endothelial factors. Which, according to their functional affiliation, are divided into those that cause contraction and / or relaxation of the muscular layer of the vascular wall (constrictors and dilators). Apparently, they are realized through and through the paths of physical and biological processes and affect physical and biological objects

In response to these effects, endotheliocytes synthesize substances that can lead to increased or decreased aggregation and adhesion of circulating blood cells in the vascular system.

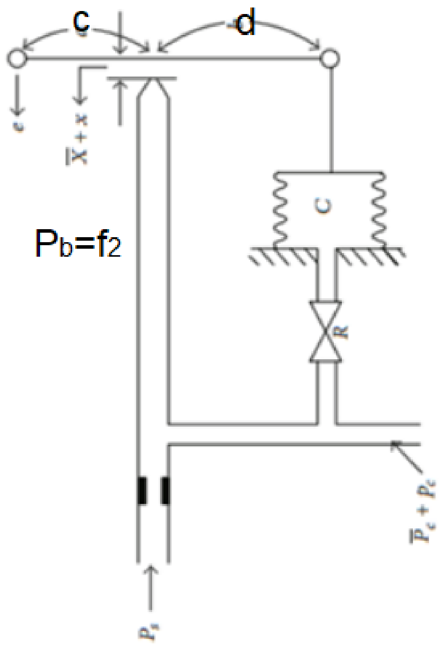


Fig 2: Pneumatic-mechanical model in the form of a "nozzle-damper-bellows" on a physico-biological control object (FBOU), as the reaction of endothelial endothelial endotheliocytes and smooth muscle cells (MMC) vessel wall (SS) to mechanical and chemical effects (and). Adapted according to source [4].

Also, it can be easily shown that for the mathematical model, the movement of the flap to the nozzle, which is inherently as the effect on the endothelial cells (endotheliocytes) of mechanical and chemical effects (Figure 2) - the following mathematical dependence is performed:

Where: c and d - lever arms (flap)

Here c and d - are the coefficients of adjustment in numerical values of mechanical and chemical effects on the endothelium, which lead endotheliocytes to: 1. Dysfunction and synthesis, advising biologically active substances, or: 2. Establish, the optimal mode of operation of endotheliocytes, in the endothelium.

Where: and in silico tuning coefficients (0.2, 0.6, 1.0)

– pharmacological coefficients, calculated by the formula equation presented as an embarrassing effect of SMSH.2 () in the physico-biological systems of automatic regulation of FBSAR on the cardiovascular system (CCC).

It is easy to see that the values of the embarrassing effect () on blood vessel cells depend on the conditional distance between endothelial cells and suma factors and , as in silico tuning coefficients affecting the walls (membranes) of endotheliocytes and smooth muscle cells (MMC).

In this particular case , there is an important incoming variable to the cell membrane of the cells of the vessel wall of the circulatory system, the blood flow in the vessels and / or endotheliocytes. Which variable, we can, stop, after the experiment as a pharmacological coefficient with the corresponding values calculated by the formula equation.

B. Structural and functional scheme of the physico-biological object of control (FBOU), as a dynamic link in the composition of the physico-biological system of automatic regulation (FBSAR)

Fig :3 shows the real structural and functional scheme of the physico-biological control object (FBOU), endothelial endotheliocytes and smooth muscle cells (MMC) vessel wall (CC) are subjected to mechanical and chemical influences according to the transfer function with the equation

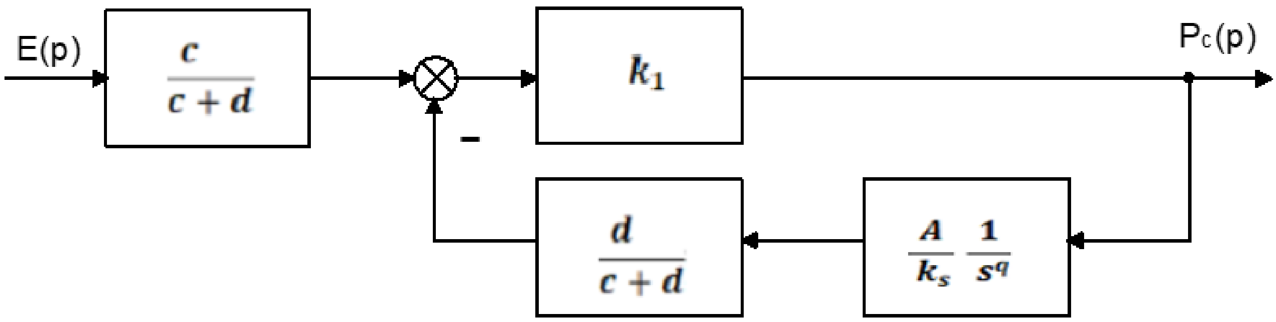


Fig:3 – Structural and functional scheme of the physico-biological object of control (FBOU), as the reaction of endothelial endothelial and smooth muscle cells (MMC) vessel wall (CC) to mechanical and chemical effects (and)

Now, the transfer function between the control pressure and the error signal can be obtained using Mason's formula as follows:

Or

I'll equate and Where: **-** Laplace's transformation to (See and Figure 4) **Laplace's** transformation to (See Figure 4)

Thus, as a result of the analysis of the method of mathematical modeling, research and design **in silico**, the construction of the basic structures of cardiovascular systems (CCC),, it was found that: the main effects on the pharmacological target of the cardiovascular system are the coefficients of adjustment of practical implemented connections and automatic regulation systems (CAP) in the theory of automatic control (TAU).

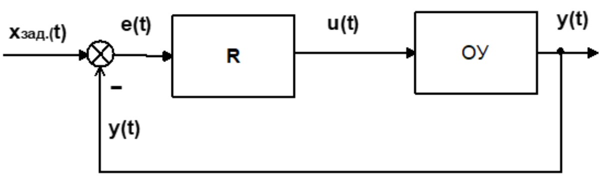
Results and Discussion

As a result of the construction in silico of the structures of the cardiovascular system (CCC) on the basis of methods of mathematical modeling of the endothelium and the model from the theory of automatic control (TAU), we built a typical automatic regulation system (CAP).

In the theory and practice of automatic control (TAU), the main elements **in the structure** of the automatic control system (CAP) are the regulator (**R**) and the control object (**OU**) (Figure 4).

In the real systemsof homeostasis of the physical organism, the nerve centers (NC) - the autonomic part of the nervous system (NS) and the central nervous system (CNS) are, the main elements in the structure of the physico-biological systems of automatic regulation (FBSAR) as a regulator (R).

Structural schemes, transfer functions and equations of the regulator (**R**) and the control object (**OP**) are built on the basis of equations and transfer functions from the types of dynamic links (inertia-free links; inertial links; oscillatory links; differentiating links and integrating links.)



Conclusion

Functional structural diagrams and their corresponding transfer functions are real objects in automatic control systems (CAP) and correspond quite to physico-biological automatic control systems (FBSAR). Structural schemes in FBSAR are related logical and functionally ordered dynamic links. They are presented as functionally related – physico-biological objects of control (FBOU), functional links (FZ) and regulators (R), and perform certain tasks to support the homeostasis of a given system, or the homeostasis of a physico-biological organism.

When conducting a practical analysis of the methods of mathematical modeling of the endothelium for the preparation of research and design in silico structures of the cardiovascular system (CCC), it was found that the main features of the experimental determination of the conditions for the implementation of the research technique are, the direction of the implementation path and extrapolation of the data obtained for the "tuning coefficients" for physico-biological automatic control systems (FBSAR).

Thus, the in-silico model of the structures of the cardiovascular system (CCC) based on the model from the theory of automatic control (TAU) is a system of interrelated components of tuning coefficients, functioning as: "pharmacological coefficients" of homeostasis on real physico-biological control objects (FBOU) and physico-biological automatic control systems (FBSAR).

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