Intelligent Big Data system based on scientific machine learning of cyber-physical systems of medical and biological processes

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Abstract

The work focuses on developing a Big Data system allowing us to process medical data intelligently, which are ingested from different sources and of various types. It aims to design biosensor devices with desired qualitative characteristics, namely their operational stability. The article suggests the mathematical representation of the discrete population dynamics and the dynamic logic of the studied models of the most advanced biosensors as biopixels arrays which are used at the analytics stage of scientific machine learning. Application software for the intelligent Big Data system for investigating the stability of cyber-physical systems for medical purposes using the R package has been developed. The software package for the intelligent Big Data system for investigating the stability of cyber-physical systems for medical applications consists of the following main software modules: unit of ingesting and processing Big Data used to identify input parameters of the model of cyber-physical systems; the software module of research of dynamic behavior of cyber-physical systems; the software module of research of dynamic logic of cyber-physical systems; the block of decision-making on the stability of cyber-physical systems; the block of visualization, lattice images of macrophage/monoclonal antibody data source, a database that receives lattice images of macrophage binding to monoclonal antibodies and a database that receives images of fluorescent biopixels. Using the software package, the results of computer simulation of mathematical models of cyber-physical systems of medical and biological processes in the form of images of macrophage, monoclonal antibodies, connections of macrophages with monoclonal antibodies, fluorescent pixels, and an electrical signal from the converter are obtained.

Keywords 1

cyber-physical system, Big Data, stability of the model, differential equations, difference equations, rectangular lattice, hexagonal lattice

1. Introduction

The most popular areas of use of Big Data in medicine are diagnostics using medical images in ophthalmology [1-3], oncology [4, 5], dermatology [6], cardiology [7]. These are the branches of modern medicine where most images are used for diagnosis.

Over the last decade, we have seen a rapid growth of digital developments, including a variety of sensors, microcontrollers, communication systems to meet societal needs. Thanks to the Internet of Things (IoT) and the use of biosensors, digital electronic health services are increasingly used every year. Biosensors play a critical role in the Internet of Things when it comes to eHealth. There are a

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number of sensors available on the market that help people monitor their daily fitness, blood glucose levels, and many sensible applications of primary diagnostics at home. In [8] the problems of safe and confidential use of the most modern biosensors for the Internet of Medical Things are considered.

The architecture of intelligent monitoring of electronic health of patients with chronic diseases is presented in [9]. Elements of the architecture include portable devices, biosensors, and smartphones for collecting medical and biological indicators [10]. The intelligent system uses scientific machine learning (SciML) as a tool for analytics in the context of complex applications across science, engineering, and medicine [11, 12]. It focuses on Big Data, obtained from various hospitals, and data obtained from the patient, to diagnose and generate warnings of critical and crisis situations. The system of health monitoring using prognostic calculations using Big Data analysis is presented in [13]. The use of Big Data in endoprosthesis is considered in [14]. Google works with US clinics to track searches for the COVID-19 pandemic and to predict in which region the outbreak will occur [15].

In 2013, thanks to an electronic medical card, which stored all the information about the client, scientists established a relationship between brain degradation and diabetes. Scientists from the University of Cape Town, thanks to a correct analysis using Big Data, analyzed the most common types of cancer and found that malignant tumors of the intestine, lung and ovary have clear genetic markers. Medical Big Data helps prevent the development of the disease at an early stage through the analysis of cardiovascular pressure, pulse, respiration and blood sugar [16, 17].

A few years ago, Apple and IBM joined forces to give IBM Watson even more structured information from the iPhone and Apple Watch. One of the most promising vectors of Big Data development in medicine is surgery [18, 19], where the relevant systems analyze all available protocols of operations in order to assess the possible risks of surgical interventions in the form of visualization in different colors. At home, Americans simply connect a stethoscope to the iPhone and send the data to their doctor. At the same time, a large cluster collects information on all patients. It is sorted by criteria and then looks for dependencies, confirm or refute myths.

Nowadays, the integration between physical resources and computing leads to the creation of complicated computing systems with distributed parameters. Such systems are controlled or managed by integrated into the Internet computing resources[20, 21]. In recent years, we have seen an interest in cyber-physical systems (CPS), which are tools for controlling and monitoring the studied indicators using computer technology, in which software is closely related to physical objects. CPS for medical applications are used to measure and analyze biochemical parameters in biological fluids, detection of cancer, markers of heart failure, pathogenic bacteria, to determine the level of contamination of food and the environment. In recent years, CPSs have been used effectively, in which the function of selective elements is performed by biosensors. Such systems are called cyber-physical biosensor systems (CPBSS), which have a number of advantages: high selectivity, stability, performance, affordable cost, the ability to use a wide range of users.

As a result of the use of CPBSS, Big Data is obtained, which requires processing and interrelation with the measured medical and biological parameters. The analytical analysis of the obtained data in the form of useful knowledge for use by software services that control the studied systems is carried out.

For Big Data analysis, SciML is used as a data-driven method for studying computer algorithms that are automatically improved through experience [22, 23].

In CPS, “experience” is usually presented in the form of data, and SciML allows you to create mathematical models based on sample data for forecasting and decision making. SciML has made significant strides in a variety of fields, including computer vision, language recognition, and control systems, as well as related scientific fields in physics, chemistry, and biology [24].

Processing data ingested from CPS of medical and biological processes is one of the important solutions which fits the “5 V’s of Big Data” characterization of Big Data [25]. The volume of such type of data grows drastically. So, the amount of healthcare data gathered from 2013 to 2020 has grown 15 times to 2314 exabytes [26]. The functioning of most CPS in medical applications is in real-type mode, corresponding to the requirements of velocity for BigData. Data sources used for medical CPS varies from numerical and literal signals (ECG, EEG, EMG, etc.) to medical images (CT, MRT, USG, etc.), which fits a variety of data sources. The veracity of medical CPS data is assured by the quality of standardized measurements used. Finally, the Value of Big Data solutions within medical

data-driven-CPS is supported by new results on diagnostics, treatment, and prophylaxis, which can be exceptionally obtained using SciML.

Algorithms and methods for processing measurement parameters in the CPS of medical and biological processes using Big Data are created on the basis of their mathematical models. Mathematical models of biosensors for CPBSS on rectangular lattice using lattice differential equations with delay have been developed [27, 28]. The mathematical models of biosensors for CPBSS on rectangular lattice using lattice difference equations with time delay are developed in the article [29]. A detailed description of the considered model is presented in [30, 31].

When developing the modern CPS with the desired qualitative characteristics we need to process the medical information of the different kinds, which corresponds to the notion of Big Data. Namely, the medical data fit the main features of Big Data such as variety, value, velocity, and veracity.

Medical data in CPBSS come from different sources and types, so in their operation it is necessary to ensure independence and operational stability. Therefore, there is a need to develop a software package for the intelligent system BigData in the study of the sustainability of medical CPS. These studies are particularly relevant for autonomy, which is defined as the improvement of enzyme activity, protein when maintained under certain conditions, as well as operational stability to ensure the performance of CPS when measuring biomedical parameters. The usefulness of the studied systems is determined by the stability of the sensitive element, which is located in the receptor, and the functioning of the corresponding components of the matrix of the system during its use.

The purpose of the study: to develop a software package for the intelligent system BigData in the study of the stability of medical CPS.

1. Mathematical models of biosensors of the intelligent Big Data system for medical aplications

1.1. Mathematical model of biosensor on rectangular lattice using differential equations with time delay

In models of lattice differential equations, the spatial structure has a discrete character and lattice dynamics is widely used in the examples considered in [30, 31] and the mathematical model of the immunosensor, which characterizes the change in the concentration of macrophages $M_{i,j}(t)$ and monoclonal antibodies $A_{i,j}(t)$ was substantiated:

$$\begin{aligned} \frac{dM_{i,j}(t)}{dt} &= (\beta - \gamma A_{i,j}(t-\tau) - \delta_{\upsilon} M_{i,j}(t-\tau)) M_{i,j}(t) + \hat{S}\{M_{i,j}\}, \\ \frac{dA_{i,j}(t)}{dt} &= (-\mu_f + \eta\gamma M_{i,j}(t-\tau) - \delta_f A_{i,j}(t)) A_{i,j}(t), \quad t > 0, \end{aligned} \tag{1}$$

where γ - the speed of detection of macrophages;

β - birth rate constant of macrophages;

τ - time delays in the formation of the macrophage-monoclonal antibody complex;

δ_M - the average rate of decrease in the concentration of macrophages;

δ_A - the average rate of decrease in the concentration of monoclonal antibodies;

η - probabilistic rate of formation of the macrophage-monoclonal antibody complex;

Δ - distance between immunopixels;

D - macrophage diffusion coefficient;

$\hat{S}\{M_{i,j}\}$ - operator of diffusion processes.

The model of the immunosensor (1) using lattice differential equations most fully takes into account all parameters of immunosensory systems, namely: to take into account when measuring the concentration of macrophages $M_{i,j}(t)$ and monoclonal antibodies $A_{i,j}(t)$ and their binding properties, constant fertility of macrophages, time delay formation of a macrophage-monoclonal antibody complex; the average rate of decrease in the concentration of macrophages and monoclonal

antibodies; probabilistic rate of formation of the macrophage-monoclonal antibody complex; the distance between the immunopixels; macrophage diffusion coefficient; diffusion process operator.

These parameters are used by immunosensory systems.

Model (1) is given by initial functions (2)

$$\begin{aligned} &M_{i,j}(t) = M^{0}_{i,j}(t) \geq 0, \quad A_{i,j}(t) = A^{0}_{i,j}(t) \geq 0, \\ &t \in [-\tau, 0), \quad M_{i,j}(0), A_{i,j}(0) > 0. \end{aligned} \tag{2}$$

For a square array $N \times N$, the discrete diffusion is used for the spatial operator, taking into account the imbalance constant n_{dsbn}

$$\hat{S}\{M_{i,j}\} = \begin{cases} D\Delta^{-2}\left[M_{1,2} + M_{2,1} + M_{i,j-1} - 2n_{dsbn}M_{1,1}\right], & i, j = 1 \\ D\Delta^{-2}\left[M_{2,j} + M_{1,j-1} + M_{1,j+1} + M_{i,j+1} - 3n_{dsbn}M_{i,j}\right], & i = 1,\ j \in \overline{2, N-1} \\ D\Delta^{-2}\left[M_{1,N-1} + M_{2,N} - 2n_{dsbn}M_{1,N}\right], & i,\ j \in \overline{2, N-1} \\ D\Delta^{-2}\left[M_{i-1,N} + M_{i+1,N} + M_{i,N-1} - 3n_{dsbn}M_{i,N}\right], & i \in \overline{2, N-1},\ j = N \\ D\Delta^{-2}\left[M_{N-1,N} + M_{N,N-1} - 2n_{dsbn}M_{N,N}\right], & i = N,\ j = N \\ D\Delta^{-2}\left[M00_{N-1,j} + M_{N,j-1} + M_{N,j+1} + M_{i,j+1} - 3n_{dsbn}M_{N,j}\right], & i = N,\ j \in \overline{2, N-1} \\ D\Delta^{-2}\left[M_{N-1,1} + M_{N,2} - 2n_{dsbn}M_{N,1}\right], & i = N,\ j = 1 \\ D\Delta^{-2}\left[M_{i-1,1} + M_{i+1,1} + M_{i,2} - 3n_{dsbn}M_{i,1}\right], & i \in \overline{2, N-1},\quad j = 1 \\ D\Delta^{-2}\left[M_{i-1,j} + M_{i+1,j} + M_{i,j-1} + M_{i,j+1} - 4n_{dsbn}M_{i,j}\right], & i,\ j \in \overline{2, N-1}. \end{cases} \tag{3}$$

Each pixel is exposed to macrophages from four adjacent pixels that are separated by equal distances Δ.

The boundary condition $M_{i,j} = 0$ for the edges of the array $i, j = 0, N+1$ is used.

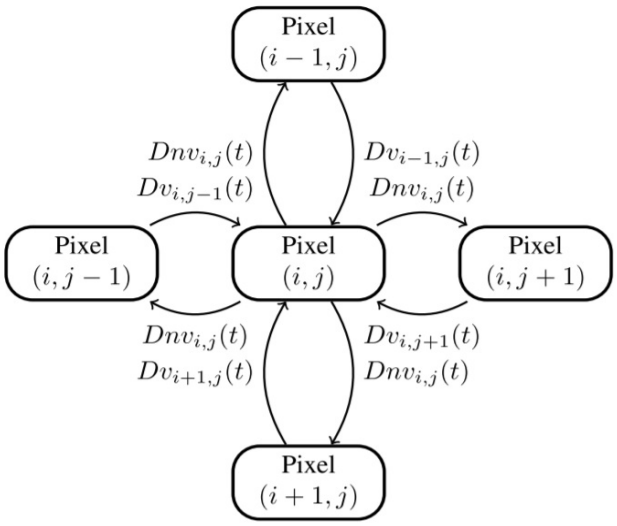


Figure 1: A rectangular grid that connects four adjacent pixels in the biosensor model using a Cartesian coordinate system

1.2. Mathematical model of biosensor on hexagonal lattice using lattice difference equations with time delay

For the intelligent Big Data system of medical and biological processes dynamics, we use the mathematical description with the help of nonlinear difference equations with delay.

The model of the biosensor on the basis of a hexagonal lattice is considered. In this case, for the numbering of biopixels (i, j, k), $i, j, k = \overline{-N, N}$, $i + j + k = 0$ the cubic coordinate system is used [32, 33].

Let $M_{i,j,k}(t)$ is the concentration of macrophages, $A_{i,j,k}(t)$ is the concentration of monoclonal antibodies in the biopixel (i,j,k); $i,j,k=\overline{-N,N}$, $i+j+k=0$.

In the model it is used next parameters:

$\gamma>0$ - the speed of detection of macrophages;

β - birth rate constant of macrophages;

τ - time delays in the formation of the macrophage-monoclonal antibody complex;

δ_M - the average rate of decrease in the concentration of macrophages;

δ_A - the average rate of decrease in the concentration of monoclonal antibodies;

η - probabilistic rate of formation of the macrophage-monoclonal antibody complex;

$\Delta>0$ - distance between immunopixels;

D - macrophage diffusion coefficient;

$\hat{S}\{M_{i,j}\}$ - operator of diffusion processes.

When colonies of monoclonal antibodies are absent, colonies of macrophages are regulated by a logistic equation with time delay:

$$M_{i,j,k}(n+1)=(1+\beta-\delta_v M_{i,j,k}(n-r))M_{i,j,k}(n), \tag{4}$$

where β and δ_v – positive numbers, and $r\geq 0$ mean latency of the negative responce of the macrophages' colonies.

The diffusion of macrophages from six adjacent pixels is considered $(i+1,j,k-1)$, $(i+1,j-1,k)$, $(i,j-1,k+1)$, $(i-1,j,k+1)$, $(i-1,j+1,k)$ i $(i,j+1,k-1)$ (Fig. 2) with diffusion speed $D\Delta^{-2}$.

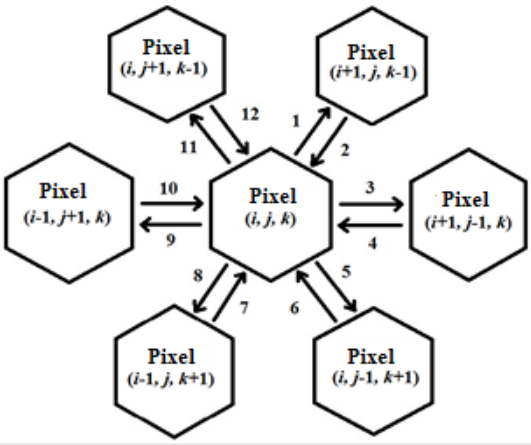


Fig. 2. Hexagonal lattice, which binds six neighboring pixels in the model of the biopixels using the cubic coordinates:

$$1,3,5,8,9,11 - \left(\frac{D}{\Delta^2}M_{i,j,k}(t)\right);\ 2 - \left(\frac{D}{\Delta^2}M_{i+1,j,k-1}(t)\right);$$

$$4 - \left(\frac{D}{\Delta^2}M_{i+1,j-1,k}(t)\right);\ 6 - \left(\frac{D}{\Delta^2}M_{i,j-1,k+1}(t)\right);\ 7 - \left(\frac{D}{\Delta^2}M_{i-1,j,k+1}(t)\right);\ 10 - \left(\frac{D}{\Delta^2}M_{i-1,j+1,k}(t)\right);\ 12 - \left(\frac{D}{\Delta^2}M_{i,j+1,k-1}(t)\right).$$

The mathematical model of late- macrophage - monoclonal antibody interaction for a hexagonal array of biopixels using based on the well-known Marchuk model [34-36] and uses the spatial operator $\hat{S}$ proposed in [37].

$$\begin{aligned} M_{i,j,k}(n+1) &= M_{i,j,k}(n)\exp\{\beta-\gamma A_{i,j,k}(n-r)-\delta_v M_{i,j,k}(n-r)\}+\hat{S}\{M_{i,j,k}(n)\},\\ A_{i,j,k}(n+1) &= A_{i,j,k}(n)\exp\{-\mu_f+\eta\gamma M_{i,j,k}(n-r)-\delta_f A_{i,j,k}(n)\},\quad n>0 \end{aligned} \tag{5}$$

where $\hat{S}\{M_{i,j,k}\}$ is a discrete diffusion for a spatial operator $\hat{S}$.

$$M_{i,j,k}(n) = M^{0}_{i,j,k}(n) \geq 0, \quad A_{i,j,k}(n) = A^{0}_{i,j,k}(n) \geq 0,$$
$$n \in [-r,0), \quad M_{i,j,k}(0), A_{i,j,k}(0) > 0. \tag{6}$$

2. Dynamic logical simulation of intelligent Big Data system for investigation the stability of CPS of medical and biological processes.

In order to simulate the dynamic logic of an intelligent Big Data system for investigation the stability of CPS of medical and biological processes, the syntax which is proposed by A. Platzer for the general CPS [38, 39]it is used. The CPS uses the Hybrid Programming Language (HP), which has more features than differential equations. Consider the dynamic logical simulation of intelligent Big Data system for investigation the stability of CPS for medical applications on the example of the mathematical model of biosensor on hexagonal lattice using lattice difference equations with time delay. Dynamic program is the first level of HP and it is defined by the following grammar:

$$a ::= M_{i,j,k}(n+1) = M_{i,j,k}(n)\exp\{\beta - \gamma A_{i,j,k}(n-r) - \delta_x A_{i,j,k}(n-\mathrm{r})\} + \hat{S}\{M_{i,j,k}(n)\},$$
$$A_{i,j,k}(n+1) = A_{i,j,k}(n)\exp\{-\mu_f + \eta\gamma M_{i,j,k}(n-r) - \delta_y A_{i,j,k}(n)\} \& \Phi_t. \tag{7}$$

where Φ_t is an evolutionary domain constraint in the form of a formula for the logic of the first order of real arithmetic

$$\Phi_t \overset{\text{def}}{\equiv} M^{\min} \leq V_{i,j,k}(n) \leq M^{\max}$$
$$\wedge A^{\min} \leq A_{i,j,k}(n) \leq A^{\max} \wedge i,j,k = \overline{-N,N} \wedge n > 0, i+j+k = 0 \tag{8}$$

The functioning of the biopixel (i,j,k) is determined by two states, with respect to fluorescence. Namely, s_{fl} is a state of fluorescence and $s_{non\,fl}$ is one of the non-fluorescence states. The use of the first order of semantics of logic and the satisfaction ratio $s\big| = L$ for the first-order formula L of real arithmetic and state s can be determined for some pixels $(i,j,k); i,j,k = \overline{-N,N}, i+j+k = 0$ states s_{fl} and $s_{non\,fl}$ as

$$s_{fl}\big| = k_{fl} M_{i,j,k}(n) A_{i,j,k}(n) \geq \Theta_{fl},$$
$$s_{nonfl}\big| = k_{fl} M_{i,j,k}(n) A_{i,j,k}(n) < \Theta_{fl} \tag{9}$$

Discrete changes occur in computer programs when they accept new values for variables. This situation occurs when a fluorescence phenomenon occurs in a pixel (i,j,k); $i,j,k = \overline{-N,N}$, $i+j+k = 0$. The state $s_{fl,i,j,k} := 1$ is assigned a value of 1 to the variable $s_{fl,i,j,k}$. This leads to a discrete, jump-like change, as the value $s_{fl,i,j,k}$ does not change smoothly, but rapidly when it suddenly changes from 1 to $s_{fl,i,j,k}$, causing a discrete jump of values $s_{fl,i,j,k}$. In this way, we obtain a discrete model of change $s_{fl,i,j,k} := 1$, except for the model of change (9).

3. Software complex of the intelligent Big Data system for investigation the stability of CPS of medical and biological processes

The software package for the intelligent Big Data system for investigation the stability of CPS of medical and biological processes consists of the following main software modules: unit of ingesting and processing Big Data used to identify input parameters of the model of CPS, the software module of research of dynamic behavior of CPS, the software module of research of dynamic logic of CPS,

the block of decision-making on stability of CPS, the block of visualization, lattice images of macrophage/ monoclonal antibody data source, a data source that receives lattice images of macrophage binding to monoclonal antibodies and a database that receives images of fluorescent biopixels.

A software package for the study of CPS phase diagrams using the R package (http://www.r-project.org/) has been developed [40]. The block diagram of the software package of the intelligent Big Data system for investigation the stability of CPS of medical and biological processes is shown in Fig. 4.

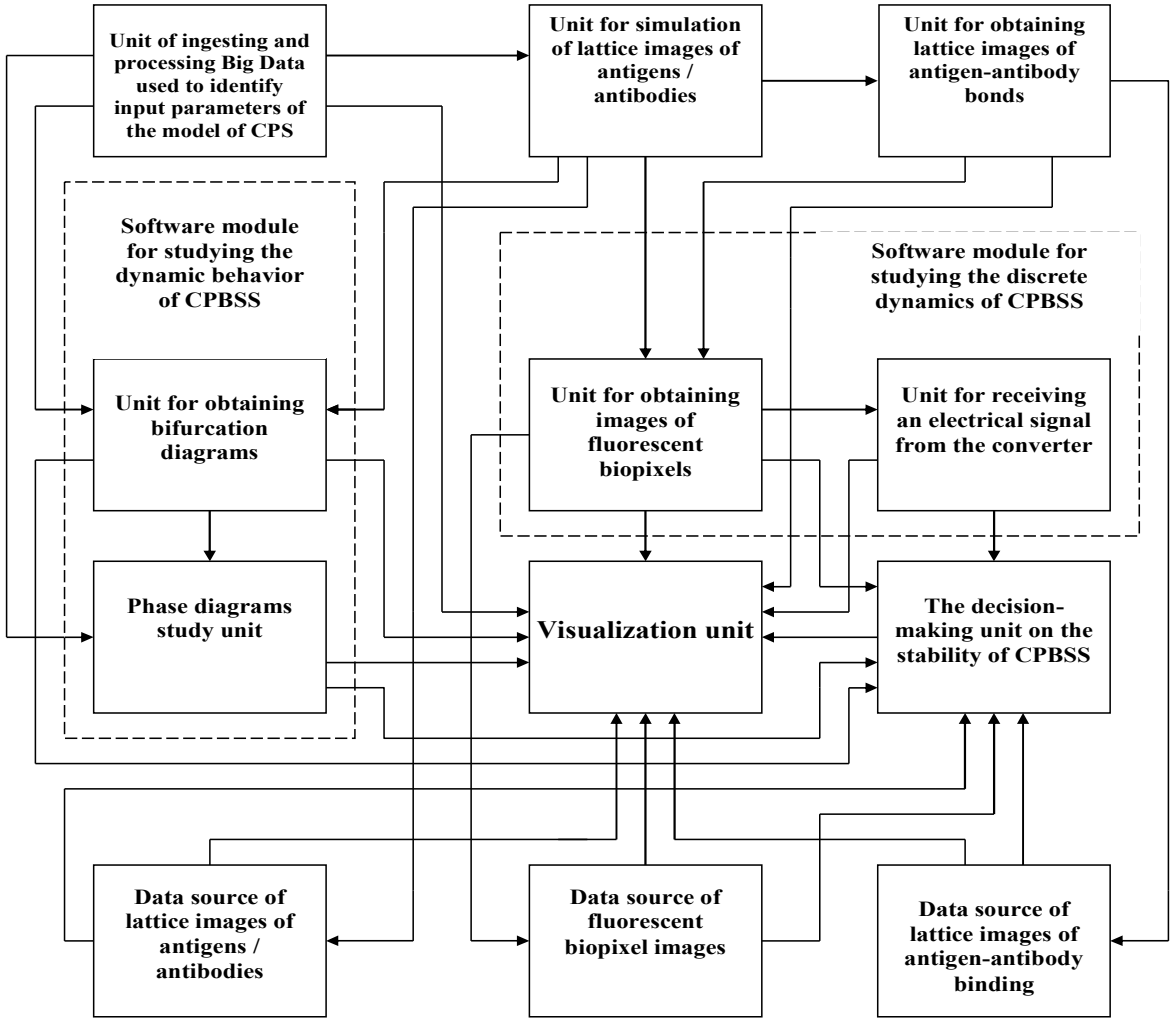


Figure 4: Block diagram of the software package of the intelligent Big Data system for investigation the stability of CPS of medical and biological processes

The software module for studying the dynamic behavior of CPS consists of blocks for obtaining bifurcation and phase diagrams. Using software to study the stability of intelligent Big Data system for investigation the stability of CPS of medical and biological processes, obtained the results of computer simulation in the form of bifurcation and phase diagrams of macrophage populations relative to monoclonal antibodies, lattice images of macrophages, monoclonal antibodies, probabilities of macrophage binding to monoclonal antibodies and monoclonal antibodies, the signal from the converter. The software module for studying the dynamic logic of CPS consists of blocks for modeling lattice images of macrophages/ monoclonal antibodies, block for obtaining lattice images of macrophage binding to monoclonal antibodies, obtaining images of fluorescent biopixels and the electrical signal from the converter. The study of CPS stability of medical and biological processes based on the Big Data intelligent system is an important data source: lattice images of macrophage/

monoclonal antibody data source, a data source that receives lattice images of macrophage binding to monoclonal antibodies, and a database that receives images of fluorescent biopixels.

4. Computer simulation of mathematical models of biosensors using an intelligent Big Data system for investigation the stability of CPS for medical applications

4.1. Parameters of mathematical models of biosensors for investigation the stability of CPS for medical applications

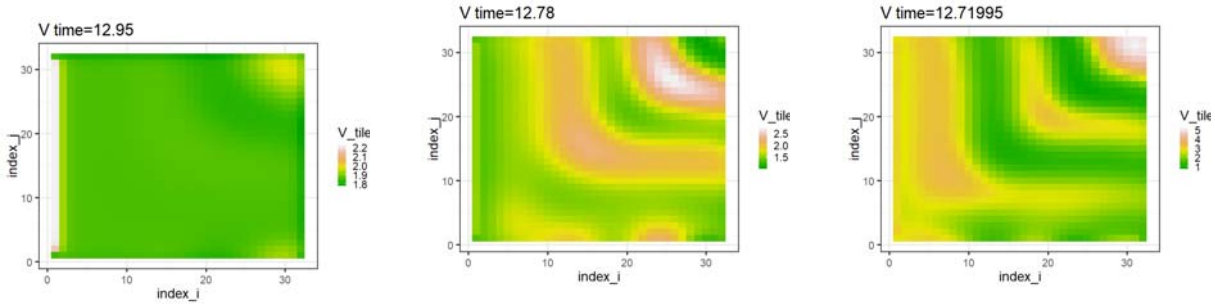
To study the occurrence of bifurcation and deterministic chaos in compartmental mathematical models of lattice type on a rectangular lattice using differential equations, models (1), (4) at $N = 4$ and values of parameters $\beta = 2\min^{-1}$, $\gamma = 2\frac{ml}{\min \cdot mkg}$, $\mu_f = 1\min^{-1}$, $\eta = 0.8/\gamma$, $\delta_\upsilon = 0.5\frac{ml}{\min \quad mkg}$, $\delta_f = 0.5\frac{ml}{\min \quad mkg}$, $D = 0.2\frac{nm^2}{\min}$, $\Delta = 0.3nm$ are considered. The concentrations of macrophages populations $V_{i,j}(t)$, $V_{i,j,k}(t)$ and monoclonal antibodies populations $F_{i,j}(t)$, $F_{i,j,k}(t)$ are measured in $\frac{mkg}{ml}$.

4.2. Results of computer simulation of mathematical model of biosensor on rectangular lattice using lattice differential equations with delay

The computer simulation was implemented for different values τ. The long-term behavior of the model (1) – (3) for $\tau = 0.05$, $\tau = 0.22$, $\tau = 0.2865$ with a set of parameter values, which are presented above is analyzed. Qualitative changes in the behavior of biopixels and the intelligent Big Data system model for the investigation of the stability of the CPS of medical and biological processes are observed.

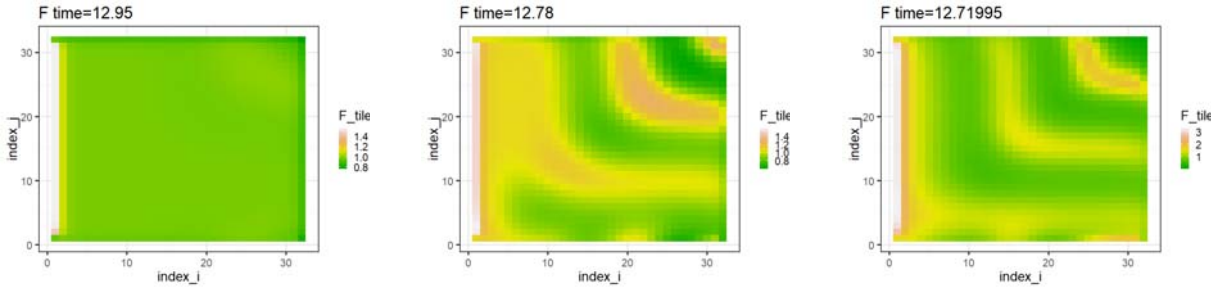
Figures 5 and 6 show the result of computer simulation of the discrete dynamics of the intelligent Big Data system for the investigation of the stability of CPS of medical and biological processes in the form of lattice images of macrophages and monoclonal antibodies in pixels of the studied system.

Figures 5 (a) and 6 (a) show the results of computer simulation of lattice images of macrophages and monoclonal antibodies in the pixels of the system (1) at $\tau = 0.05$, which corresponds to a stable focus. For $\tau = 0.22$ there is a less pronounced (Fig. 5 (b) and Fig. 6 (b)), and for $\tau = 0.2865$ more pronounced traveling wave of monoclonal antibodies, which is presented in Figures 5 (c) and 6 (c).



a) b) c)

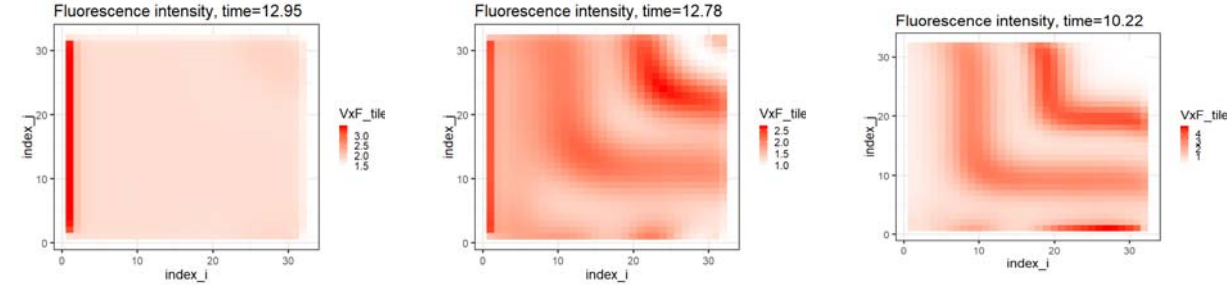
Figure 5: Lattice images of macrophages in pixels of system (1) at $\tau = 0.05$ (a), $\tau = 0.22$ (b), $\tau = 0.2865$ (c)



a) b) c)

Figure 6: Lattice images of monoclonal antibodies in pixels of system (1) at $\tau = 0.05$ (a), $\tau = 0.22$ (b), $\tau = 0.2865$ (c)

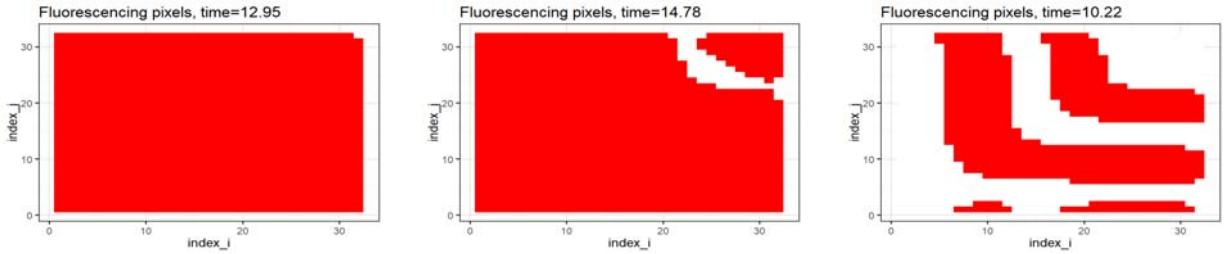
In the second stage of computer modeling of intelligent Big Data system for investigation of the stability of CPS of medical and biological processes lattice graphs are used on which for each pixel the probability of contact of macrophages with monoclonal antibodies, as $V_{i,j} \times F_{i,j}$ at $\tau = 0.05$, $\tau = 0.22$, $\tau = 0.287$ is presented. They are shown in Figures 7 (a - c).



a) b) c)

Figure 7: Lattice images of connections of macrophages with monoclonal antibodies in pixels of system (1) at $\tau = 0.05$ (a), $\tau = 0.22$ (b), $\tau = 0.2865$ (c)

Graphs of fluorescent pixels are shown in Figures 8 (a - c).

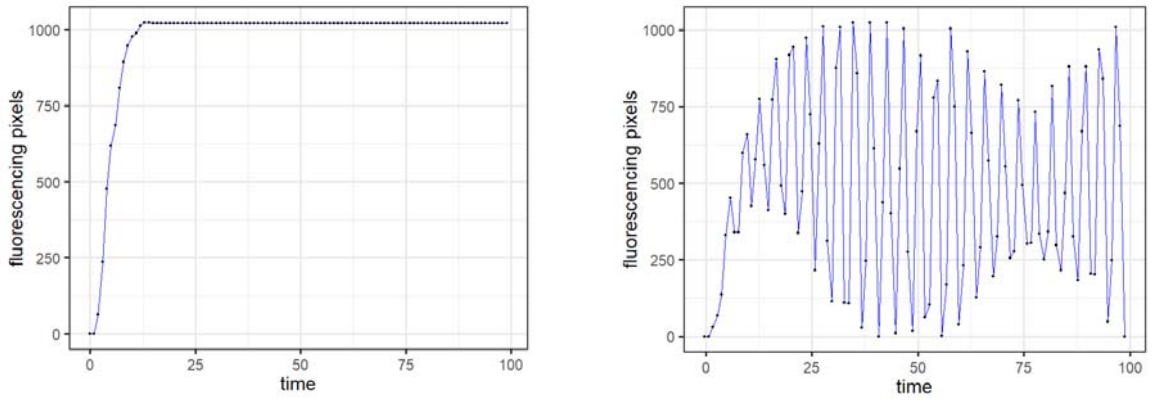


a) b) c)

Figure 8: Fluorescence image of system (1) as a result of numerical simulation at $\tau = 0.05$ (a), $\tau = 0.22$ (b), $\tau = 0.2865$ (c)

Figure 8 (a) shows the result of numerical simulation of system (1) at $\tau = 0.05$, which corresponds to a stable focus. For $\tau = 0.22$ there is a less pronounced (Fig. 8 (b)), and for $\tau = 0.2865$ it is more pronounced traveling wave of fluorescent pixels, which is shown in Figure 8 (c). Figure 8 (c) shows the result of numerical simulation of system (1), which corresponds to the approach to the limit cycle (there is a traveling wave of fluorescent pixels). In the case $\tau = 0.2865$, chaotic behavior is observed, which begins with wave-like changes in fluorescent pixels (Fig. 8 (c)) and quickly progresses to chaotic changes. Figure 8 (c) shows the result of numerical simulation of system (1), in which a chaotic wave of fluorescent pixels is observed.

To control the measurement process in the intelligent Big Data system for investigation of the stability of the CPS for medical applications, the result of computer simulation of the electrical signal from the converter (Fig. 9 (a, b)), which characterizes the number of fluorescent pixels at values of $\tau = 0.05$, $\tau = 0.2865$ plays an extremely important role. Analyzing the type of electrical signal in Figure 9, we see that when the value τ changes qualitatively changes the behavior of the pixels and the whole intelligent Big Data system to investigate the stability of the CPS for medical and biological applications. In Figure 9 (a) there is a steady state at $\tau = 0.05$. In Figure 9 (b) ($\tau = 0.2865$) a traveling wave of non-fluorescent pixels is clearly visible.



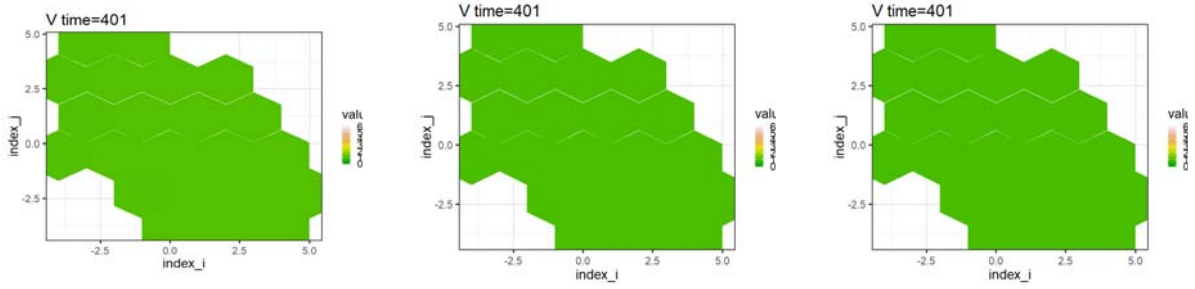
a) b)

Figure 9: Electrical signal from the converter, which characterizes the number of fluorescent pixels at $\tau = 0.05$ (a), $\tau = 0.2865$ (b)

As shown by numerical analysis, fluorescent states in biopixels change according to the laws of discrete dynamics. The threshold value for fluorescence is $\Theta_{fl} = 1{,}5$. Taking into account the continuous dynamics of the immunological response, each biopixel is considered as a CPS.

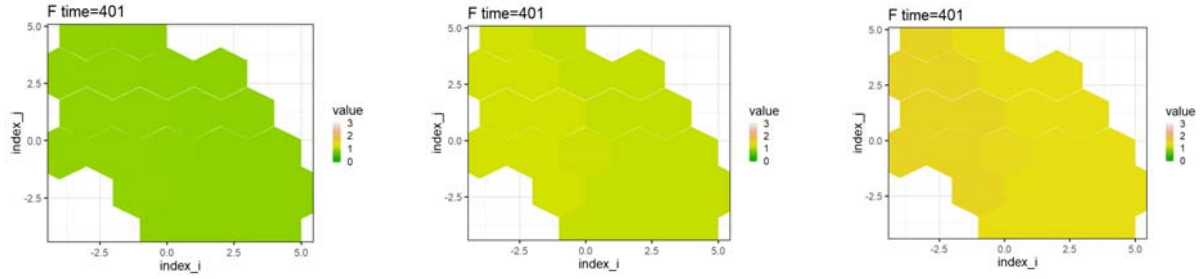
4.3. Results of computer simulation of mathematical model of biosensor on hexagonal lattice using lattice difference equations with delay

The long - term behavior of model (4) at $r = 5$, $r = 17$, $r = 22$ with a set of parameter values, which are presented above (Fig. 10 - 14), is analyzed. We observe qualitative changes in the behavior of biopixels and the biosensor model on hexagonal lattice using lattice difference equations with delay in general. Figures 10 and 11 show the first stage of computer modeling of discrete dynamics of an intelligent Big Data system for investigation of the stability of CPS of medical and biological processes in the form of lattice images of macrophages and monoclonal antibodies in pixels of the studied system. Figure 10 (a) shows the result of numerical simulation of system (4) at $r = 5$, which corresponds to a stable focus. For $r = 17$ there is less pronounced (Fig. 10 (b)), and for $r = 22$ more pronounced wavy changes in the lattice images of macrophages and monoclonal antibodies in the pixels of the system (4), as shown in Figures 10 (c).



a) b) c)

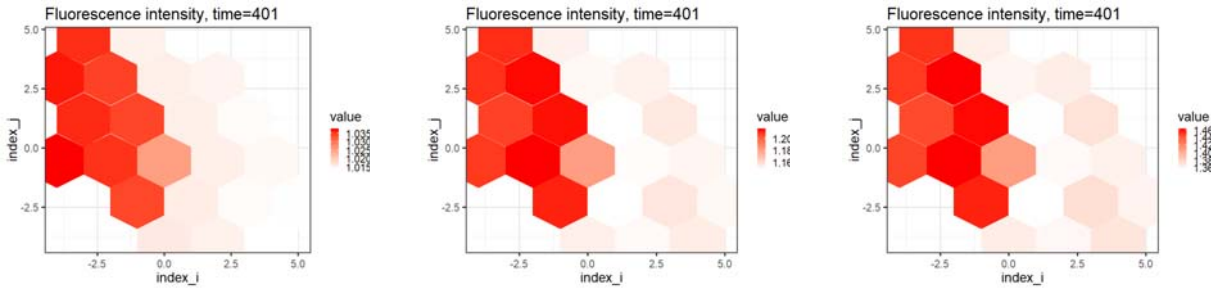
Figure 10: Lattice images of macrophages in pixels of system (4) at $r = 5$ (a), $r = 17$ (b), $r = 22$ (c)



a) b) c)

Figure 11: Lattice images of monoclonal antibodies in pixels of the system (4) at $r=5$ (a), $r=17$ (b), $r=22$ (c)

In the second stage of computer modeling of the intelligent Big Data system, lattice graphs were used to investigate the stability of the CPS of medical and biological processes. Firstly, the corresponding graphs are constructed, on which for each pixel the image of probability of contact of macrophages with monoclonal antibodies, as $V_{i,j,k} \times F_{i,j,k}$ at $r=5$, $r=17$, $r=22$ is presented in Figure 12 (a - c).



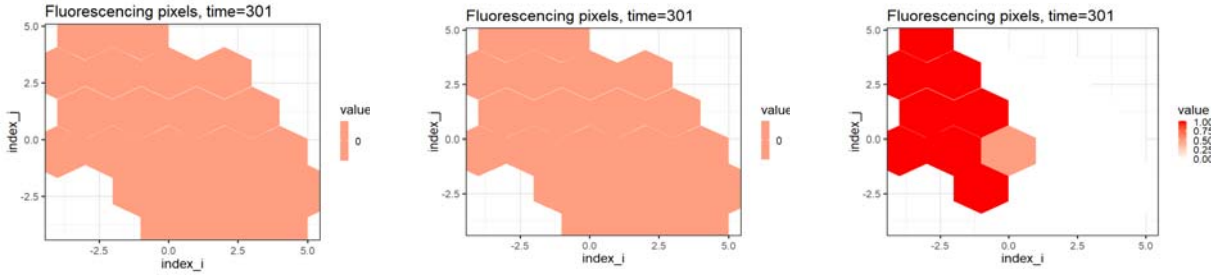
a) b) c)

Figure 12: Lattice images of macrophage- monoclonal antibody binding in pixels of system (4) at $r=5$ (a), $r=17$ (b), $r=22$ (c)

Figure 12 (a) shows the result of numerical simulation of system (4) at $r=5$, which corresponds to a stable focus. For $r=17$ there is less pronounced (Fig. 12 (b)), and for $r=22$ more pronounced wavy changes in the images of the probability of contact of macrophages with monoclonal antibodies of system (4), as shown in Figure 12 (c).

In the third stage of computer modeling of the intelligent Big Data system for investigation of the stability of CPS of medical and biological processes, lattice graphs of fluorescent pixels were obtained based on the fulfillment of condition (6), which are shown in Figures 13 (a - c).

Figure 13 (a) shows the result of numerical simulation of system (4) at $r=5$, which corresponds to a stable focus. For $r=17$ there is a less pronounced (Fig. 13 (b)), and for $r=22$ - it is more pronounced traveling wave of fluorescent pixels of the system (4), which is shown in Figure 13 (c).

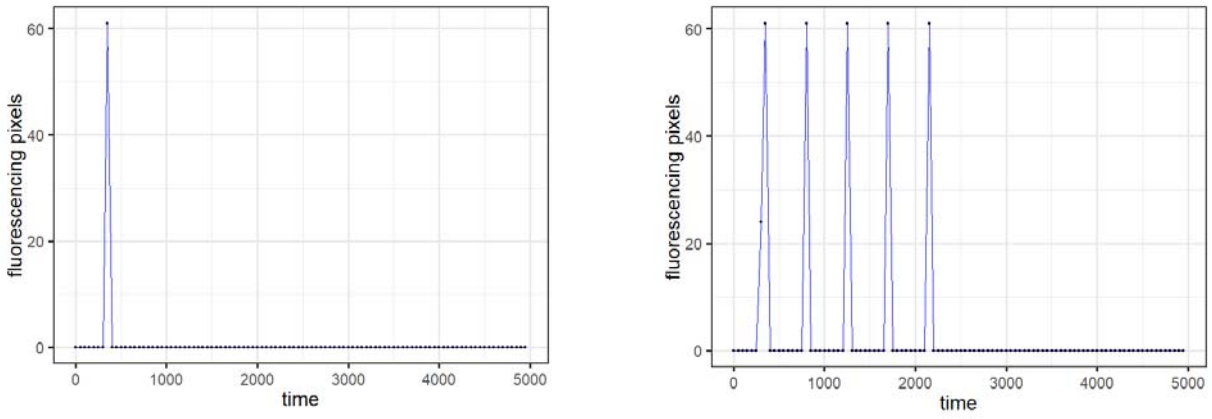


a) b) c)

Figure 13: Fluorescence image of the system (4) as a result of numerical simulation at $r=5$ (a), $r=17$ (b), $r=22$ (c)

Hopf bifurcation is observed with increasing time delay [41]. Figure 13 (c) shows the result of numerical simulation of the system (4) at $r = 17$, which corresponds to the limit cycle (there is a traveling wave of fluorescent pixels). In the case $r = 22$, chaotic behavior is observed, which begins with wave-like changes in fluorescent pixels (Fig. 13 (c)) and quickly turns into chaotic changes.

Figure 14 shows the electric signal from the converter (Fig. 14), which characterizes the number of fluorescent pixels at $r = 17$, $r = 22$.



a) b)

Figure 14: Electrical signal from the converter, which characterizes the number of fluorescent pixels at $r = 17$ (a), $r = 22$ (b)

To control the measurement process using an electrical signal to an intelligent big data system for investigation of the stability of the CPS of medical and biological processes is extremely important the result of computer simulation.

Analyzing the type of electrical signal in Figure 14, we can conclude that changing the value qualitatively changes the behavior of the pixels and the entire biosensor model based on lattice difference equations. In Figure 14 (a) ($r = 17$) occurs, and in Figure 14 (b) ($r = 22$) there is a traveling wave of non-fluorescent pixels. The threshold value for fluorescence is $\Theta_{fl} = 1{,}5$.

A two-dimensional array of biopixels was used to develop the dynamic logic of an intelligent Big Data system to investigate the stability of the CPS of medical and biological processes on a hexagonal lattice using delay equations. As shown by the results of numerical analysis, fluorescent states in biopixels change according to the laws of discrete dynamics.

5. Conclusion

In the work, the general scheme of the cyber-physical sensor system proposed in [42] was extended to the usage of Big Data. Peculiarities of immunosensors functioning are taken into account in CPS mathematical models. According to the laws of discrete dynamics, lattice images in immunopixels are modified. The proposed mathematical models take into account the interaction of immunopixels through the diffusion of macrophages.

The intelligent Big Data system uses the discrete dynamics of macrophages and antibodies, which is based on dynamic logic, to study the stability of CPS in medicine. The classes of rectangular lattice using differential equations or hexagonal lattice using difference equations are used in the work as modeling of the interaction of macrophages and monoclonal antibodies in immunopixels. This also takes into account the presence of macrophage and monoclonal antibodies colonies, that are localized in pixels, as well as the diffusion of macrophage colonies between pixels using the R package.

According to a series of experiments of intelligent Big Data system for investigation of the stability of CPS of medical and biological processes using lattice differential equations with delay it is established that in the case of using a rectangular lattice at constant time delay $\tau \in [0, 0.22]$ the solution of the studied system is a stable focus. When $\tau = 0.23$ (in the case of a rectangular lattice) there is a Hopf bifurcation and all subsequent trajectories correspond to stable boundary cycles for all

imunopixels. With a further increase in the delay constant τ, chaotic behavior of the CPS of medical processes occurs on the basis of lattice differential equations with time delay.

According to the results of a series of experiments of intelligent Big Data system for investigation of the stability of CPS of medical processes using lattice difference equations with delay it is established that in case of using hexagonal lattice at $r \in [0,16]$ the solution of the investigated system tend to endemic states, which are a stable focus. For $r = 17$ (in the case of a hexagonal lattice) there is a Hopf bifurcation and all subsequent trajectories correspond to stable boundary cycles for all imunopixels. With a further increase in the delay constant r, chaotic behavior of the CPS occurs on the basis of lattice difference equations.

The developed computer programs for the study stability of intelligent Big Data system for investigation the stability of CPS of medical processes in the form of phase diagrams, lattice images of macrophages / monoclonal antibodies, lattice images of macrophage binding to monoclonal antibodies, images of fluorescent imunopixels and the electrical signal from the converter should be used in research, design organizations, medical and laboratory centers in the development and testing of cyber-physical systems of medical processes.

In the following researches is necessary to offer mathematical models of intelligent systems of Big Data on the basis of other geometrical structures and to carry out research of their stability.

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