From Compartments to Agents via Fuzzy Models - Modeling and Analysis of Complex Behavior of Physiological Systems

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***Abstract* – It is well-known that analytical modeling and computer simulation of the physiological systems is a complex problem with a great number of variables, equations, and non-linear relations. There are several approaches for such modeling. One of them is so-called compartment modeling. Each compartment is assumed to be a homogeneous entity, within which modeled entities are equivalent. Another approach is multi-agent modeling, which consists of creating agents with a more complex structure in comparing with the compartment and a more complex logic of behavior and communication. In the paper, we decided that before building a multi-agent model to try to describe the communication of the system elements using the rules of the class 'state-action' and transferring such relations to the properties of the agents. In order to analyze the dynamics of the behavior of the multi-agent system, the matrix description method was proposed. As an example, we investigate in the article the different models of the insulin-glucose physiological system.**

Keywords – multiagent system; agent; linear algebra; matrix.

I. INTRODUCTION

The models used for modeling of any kinds of physical phenomena are the tools utilized to obtain an answer to questions concerning the tested system, without the need for performing the actual experiment. Among the variety of models, i.e., psychological, word or physical models, there are also mathematical models whose relations observed in the system are described by mathematical formulas. The possibility to perform such experiments is called simulation (lat. simulare – simulate). It is a cheap and safe alternative or a complement to experiments with the system.

The quality of simulation's results depends entirely on the quality of the model. Fundamentally, there are two approaches to building a model representing a particular system. The first type of approach is based on the knowledge taken from literature or experience of experts in each domain and could be used for building more and more precise description of the investigated phenomenon (more complex models are generated). The second one is based on observation of the phenomenon and its behavior on one level of description (using similar agents) and after that building the model and identification of parameters (agent-based approach).

The created model in both approaches needs to be described in a handy form, especially if one wants to analyze it with the use of digital machines. Having the model built, it is necessary to verify the correctness of obtained results. The credibility of the results provided by the model can be acquired using verification or validation.

This paper focuses on the use of MAS a multi-agent system (MAS) for the modeling of the insulin-glucose system responsible for the blood glucose homeostasis. Even by designing the simplest model based on the multi-agent paradigm, one must rely on a complex analysis of interactions between agents. For this reason, there is not one general formalism of description of these interactions, which would additionally allow an easy analysis of the functioning of such a multi-agent system. In most cases, the used approaches are chosen depending on the category of the problem that is solved by the system. If MAS was designed to address the issues of game theory, then this formalism would be used to analyze the multi-agent system. When MAS was created for optimization problems, these problems will be used to analyze this system [9,14]. What is presented in this paper is a demonstration of the use of two modeling techniques for the general description of a multi-agent system. On one hand, the theory of compartment models has been used to describe the interaction between the different body regions, called compartments. On the other hand, graph theory introduces a general and universal tool for describing the interaction between beings that can represent any mathematical or physical concept. Combining these two techniques allows us to describe the interaction between agents in MAS in two ways. Firstly, it could help to describe the dynamics of the entire multi-agent system, showing the connections between agents, their behavior, and the ability to investigate the whole system. Secondly, it makes possible to include in the same formalism the information associated with each agent. This should be understood as the ability to get information, about which behavior is implemented in the body of the agent, which is used to communicate with the environment, and which is only the internal behavior of the agent. One can also get information, about which agents are receivers of the messages and, which are senders of those messages.

The proposed approach allows describing MAS in two complexity scales – the system as a whole and the agent and its impact on the system. The proposed advantage is a technique, which can extend the behavior of compartments using fuzzy logic and make their behavior more complex by describing their internal structure using agent description [1]. We illustrate the MAS description and communication of the glucose homeostasis. The selected analytical model (Stolwijk-Hardy model [11]) was converted to MAS in a lossless fashion. As a result, individual members of this model became the determinants of behavior of individual agents, and in addition, the analysis of such model was maintained by compartmental methods.

The structure of the paper is following. Section II describes the compartment models and their applications in physiologic systems. In Section III we introduce the fuzzy logic models and illustrate them in the example of the insulin-glucose system. This model will be a base of agent's behavior in the next section.

Section IV gives a short introduction to multi-agent systems and draws attention to components of agents and their communication standards. In the next section, the matrix representation of MAS is proposed. Section VI illustrates the authors' approach with two simple examples. The conclusion and references summarize the article.

II. Compartment systems

The concept of a compartment is not unambiguous and may represent different features depending on what is being discussed. Usually, the compartment describes the structures of a living organism characterized by similar properties in relation to the test substance [5]. The compartments may be either separate areas of the body or substances. In the first case, the compartment can be considered an organ or intercellular space, in the latter case, it may represent blood plasma. If the test substance is in the biological system in several areas of the organism and it is possible to determine its movement between these areas and changing its concentration, then such areas can be considered as separate compartments (Figure1). The description of the transport of substances in the body is considered for the mass balance (or concentration) in individual compartments. The main reason for using this description is the ability to determine the time course of substance exchange streams between compartments and between the body and the environment.

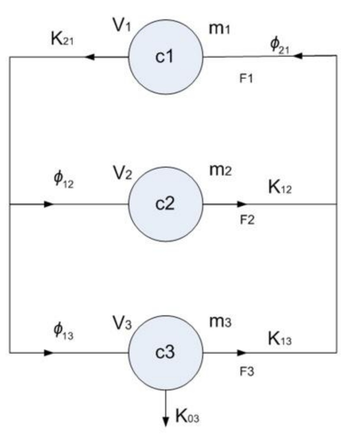

Figure 1. An example compartment model (the model has three compartments).

The considered models are constructed assuming the constant volume of compartments. In this case, the mass of substance in the compartment is proportional to its concentration. The equations describing the transport can be summarized for both mass and concentration. The transition from the first description to the second one consists only in dividing both sides of the equation by a constant factor, which is the volume of the compartment.

Considering the *i*-th compartment, the mass of substances in this compartment can be changed as a result of the algebraic summation of the input and output streams of this compartment:

$$\frac{dm_i(t)}{dt} = \sum_{\substack{j=0\\ j\neq i}} \phi_{ij}(t) - \sum_{\substack{j=0\\ j\neq i}} \phi_{ji}(t), \; i = 1,2,\dots,n \quad (1)$$

where $\phi_{ij}(t)$ denotes an input stream flowing from the *j*-th compartment to the *i*-th compartment; $\phi_{ji}(t)$- the output stream flowing from the i-th compartment to the j -th compartment; *n* - a number of model compartments.

By grouping the streams in the right order: resultant interconnection exchange rates, the elimination stream, the dosing flow and considering the biological availability F_i equation (1) for the mass balance of the *i*-th compartment can have the form:

$$\frac{dm_i(t)}{dt} = -\sum_{\substack{j=1\\ j\neq i}} \phi_{ij}(t) + \sum_{\substack{j=1\\ j\neq i}} \phi_{ji}(t) - \phi_{0i}(t) + F_i d_i(t),$$
$$i,j = 1,2,\dots,n \quad (2)$$

The subscript 0 denotes the connection of a given compartment with the external environment, where $\phi_{i0}(t) = F_i d_i(t)$ is the substance dosing flow to the *i*-th compartment, and ϕ_{oi} is a stream of elimination flowing out of the *i*-th compartment. Biological availability F_i is a fraction of the given dose $d_i(t)$, e.g., a medicinal substance that has been absorbed into the *i*-th compartment. This parameter meets the condition $0 \leq F_i \leq 1$. In cases of linear pharmacokinetics, this equation acquires the features of a differential linear equation. The following types of linear pharmacokinetic models can be distinguished:

- full-time or part-time,
- without delay or with a delay.

In linear stationary models, the streams are of the donor type, i.e., they form a function of mass $m_j(t)$ in the compartment, from which they flow and are proportional to this mass:

$$\phi_{ij}(t) = k_{ij}m_j(t)$$

where k_{ij} is the constant speed of exchange.

The counterpart of equation (2) is a linear differential equation with constant coefficients:

$$\frac{dm_i(t)}{dt} = -\sum_{\substack{j=1\\j\neq i}} k_{ij}m_i(t) + \sum_{\substack{j=1\\j\neq i}} k_{ji}m_j(t) - k_{0i}m_i(t) + F_i d_i(t) i, j = 1,2,\dots,n \quad (3)$$

where: k_{ji}, k_{ij}, k_{0i} are constant inter-compartment exchange rates and elimination velocities, respectively.

In the case of the two-compartment model (Figure 2),

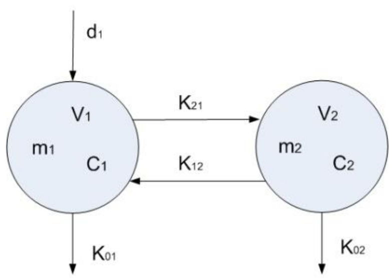

Figure 2. An example of the two-compartment model.

the equations describing the mass balance take the form:

$$\frac{dm_1}{dt} = -(k_{01} + k_{21})m_1(t) + k_{12}m_2(t) + F_1 d_1(t),$$

$$\frac{dm_2}{dt} = k_{21}m_1(t) - (k_{02} + k_{12})m_2(t). \quad (4)$$

In the general case of a multi-compartment system, the system of equations looks like this:

$$\frac{d\mathbf{m}(t)}{dt} = \mathbf{A}\mathbf{m}(t) + \mathbf{F}\mathbf{d}(t) \quad (5)$$

$$\mathbf{c} = \mathbf{C}\mathbf{m}(t) \quad (6)$$

satisfying the initial conditions:

$$\mathbf{m}(t = 0) = \mathbf{m}(0)$$

The solution of equation (3) is defined by the formula:

$$\mathbf{m}(t) = e^{\mathbf{A}t}\mathbf{m}(0) + \int_0^t e^{\mathbf{A}(t-\tau)}\mathbf{F}\mathbf{d}(\tau)d\tau \quad (7)$$

Below there is an example of such a model for the regulation of the insulin-glucose system [13] (Bergman and Cobelli model)

$$\frac{dg}{dt} = -[a_1 + x]g + a_1 G_B,$$
$$\frac{dx}{dt} = -a_2 x + a_3[i - I_B], \quad (8)$$
$$\frac{di}{dt} = a_4[g - a_5]^{+}t - a_6[i - I_B],$$

in which the test substances are insulin and glucose, which levels we denote by i and g, respectively. Depending on the parameters of the model (8), simulations, as well as analyzes of the normal state and diseases of diabetes can be made.

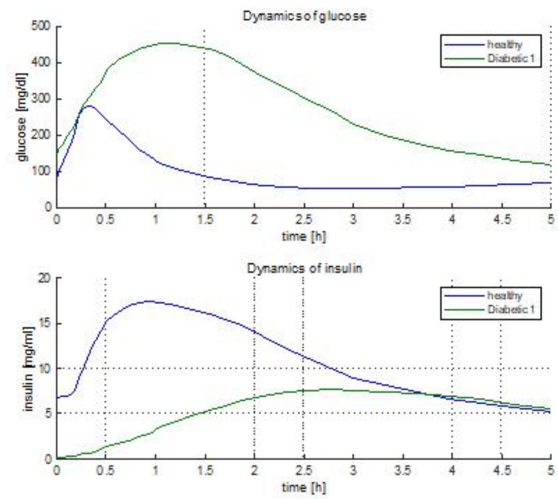

Figure 3. An example of insulin-glucose dynamics for a healthy person and person with diabetic I

Analysis of the dynamics of a multi-compartment system is given by the state equations (5), the output equations (6) consists in examining the features of solving (7), controllability and stability by analyzing the eigenvalues of the fundamental matrix A. Usually, such analysis is carried out by using the Laplace transform.

The optimization of the systems (5), (6) depends on calculating the given dose $\mathbf{d}(t)$, by means of which the quality functional for the solution (7) is minimized, for example, the preservation of a given mass change program $\mathbf{m}(t) \to \mathbf{m}^*(t)$. Well-known methods of control theory allow a solution, in which regulators are used, which are "tuned" through the selection of appropriate settings. Thus, we apply the classic methods of analysis and optimization.

The advantages of the compartmental model can be described in a uniform description of all organs that communicate with each other by means of substance transfer. The disadvantages of such a description can be the inability to describe hierarchical models and the difficulty in estimating the values of all parameters in the case of a non-linear model.

III. Fuzzy Logic Models

Biological systems can be described using a quantitative or qualitative way. Unfortunately, the quantitative approach using the compartmental description and linear models (5) and (6) does not bring the desired results. Due to the non-linearity of physiological processes, the complexity and uncertainty of the biological system and the occurrence of delays and measurement deviations, it is difficult to build a model with correctly selected parameters. These specific features of the biological system force the use of a different type of modeling.

Qualitative models are relatively simple and require basic knowledge about the modeled system to correctly map it. Quantitative models simulate the analyzed system very precisely, but they require knowledge of accurate kinetic data, which are sometimes not known satisfactorily or are simply missing. There is one more approach to building models - it is a semi-quantitative approach that uses tools such as fuzzy systems and fuzzy logic [4]. They allow the description of the system in a satisfactory way even when the data related to the kinetics of the biological process are not complete. This incompleteness can also be seen as the external and internal variability of the biological system. The assumptions that should be met by the modern model of the biological system are presented in the article by Parker [8], in which the author lists the elements necessary for such a model like that: prognostic skills within the input-output process, the ability to perform calculations using the Internet for control and optimization.

The use of this type of modeling comes to combining functional blocks in a proper way (Figure 4) and implementing the methods used in a given simulation technique in their structure.

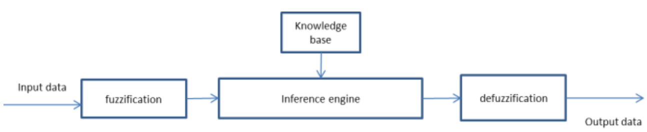

Figure 4. Fuzzy logic model.

The general principle of creating a system consists in breaking the model into several functional blocks:

- input block – responsible for entering heterogeneous input data into the system and their conversion to the internal format (for fuzzy logic this process is a fuzzyfication),
- processing block – processing of the received information using a knowledge base for this purpose - rules of fuzzy logic (for fuzzy logic these will be inference procedures),
- output block – the transformation of the calculation result generated in the processing module to the format of the user-understandable model or to the format used by the rest of the model (for fuzzy logic this process is defuzzyfication).

To create a system, it is worth to use graph models, in which the nodes are individual elements, and the edges are a substance and information transferred from one element to another.

For each of the individual organs of the insulin-glucose system, we create sets of rules describing its behavior according to the knowledge of its internal state and parameter states in other organs.

The rule has a structure of recursive relationships that combine the state at a discrete time k and k+1:

$$\textit{If } X_{1k} = NB \textit{ and } X_{2k} = ZE \textit{ and} \ldots X_{jk} = NS \textit{ Then } X_{i,k+1} = PS, \quad (9)$$

where X_{jk} are variables that characterize the content of substances in the body j, and NB-negative big, NS-negative small, ZE-zero, PS-positive small, ... are linguistic variables that use the membership functions to determine the full range of the value of the respective substance.

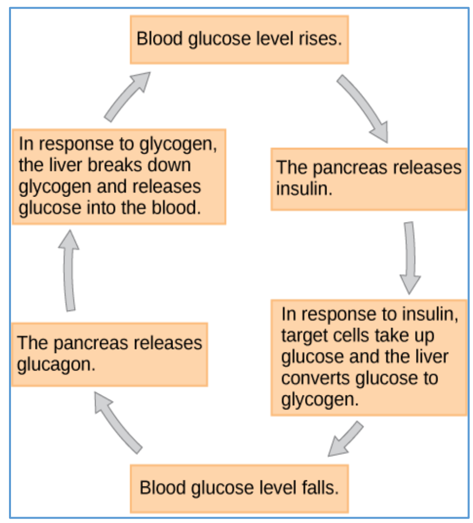

Figure 5. Dynamic of glucose transportation.

Type (9) rules allow creating dynamic relationships, for example, for the insulin-glucose system (Figure 5). Each block of the system contains a model of fuzzy logic.

One of the main advantages of the fuzzy model is a very simple way of describing the communication of organs of the physiological system in the form of rules (9) and the selection of parameters as membership functions of linguistic variables. The disadvantage of such a system is the difficulty of analyzing and creating the optimal control of such a system.

IV. Multi-Agent Systems

We present here the basic ideas concerning multi-agent systems.

A. *Concept of the multi-agent system and agent*

MASs are complex systems of agents communicating and cooperating with each other. This construction of the systems enables solving problems of a diffuse or complex calculation. In the studies applying multi-agent systems, the concept of an agent is presented as an autonomous object having the initiative of action based on the observation of the environment, in which it is located. It also has the ability to use the resources of the environment and the motivation to solve the problem it has to face. Such definition of the agent forces it to have inputs called sensors (through which it will be able to receive signals from the environment) and effectors, which can be used to influence the surrounding environment. The most important task of the agent is to decide, which of the possible courses of action is best, at the time of acquired knowledge about the problem, in order to achieve the goal.

The issue „agent" is wide and diverse. Nowadays, the term is so broadly used that is best described as comprising a heterogeneous body of research and development [2,7]. Different communities refer to it in various ways. Some scientists will characterize agents as initiatives and reactivity of objects; others emphasize independent learning and communication skills. What can also be invoked is the characteristic that unifies modeling agent the most – it is their decentralization. An extensive discussion of multi-agent systems can be found in positions [15,12].

In contrast to the dynamic system or actions based on models, MAS does not have a special place of centralization where the dynamics of the system is fixed. In addition, the global behavior of the whole system is determined based on the individual behavior of all agents. Each agent has its own internal behavior as a set of rules and behaviors for interacting with the environment and other agents. This description creates a dynamic interaction of agents based on the rules.

In many situations, there is a doubt linked to the lack of understanding of the philosophy of using multi-agent systems and returning toward object-oriented programming. What is characteristic of multi-agent systems can be presented in the following subparagraphs:

- Agents possess internal awareness and defined goals to be achieved. The goals can, but do not have to be identical to the objectives of the other agents who are in the same environment. In such case, information obtained from another agent can be considered only if it is coincident with its own objective.
- An agent is a dynamic instance, which adapts its activity to instantaneous changes in the environment and has certain fixed parameters and characteristics only for it that do not change regardless of the extent of the changes observed in the environment.
- Each agent possesses at least one strand, which is responsible for its behaviorism.

The general difference between instance of an agent and an object lies in the fact that the object has variables that change, while the agent variables can be changed only when the agent accepts the request of the sender to change the value of a variable in an immediate way or after the act of negotiation.

B. Communication in multi-agent system

In an environment where there is more than one agent, there must be a mechanism for the exchange of information between the environment and the agent, and between agents. Communication mechanisms are essential for the agents grouped in structures that facilitate co-operation so that they could achieve their goals. Since the multi-agent environments [6,10] are dynamic environments, it is necessary to introduce a mechanism that would allow for informing the agents of the existence of other participants in the system. The literature [3] distinguishes the following approaches:

- Yellow pages, where agent can place information about services it provides,
- White pages – the list of all agents in the environment,
- Broker – intercessory agent.

To create a message and then send it to another agent in such a way they can receive it and understand it, it is necessary to define a common communication language. It should be noted that the communication language, which is independent of the field, is separated from the language of messages content. Among the communication standards the most popular ones include:

- KQML (Knowledge Query and Manipulation Language),
- ACL (Agent Communication Language).

Among the examples of the language of message content, the following should be distinguished:

- KIF (Knowledge Interchange Format),
- FIPA standards:
  - SL (Semantic Language),
  - CCL (Content-Language).

Having a tool for communication, agents can communicate with each other to achieve a common or an opposing goal. In the first case, we have to deal with the concept of co-operation, in the second case - with the competition concept. As a rule, multi-agent systems are designed to solve complex problems, in which agents have control (or can observe) only over a certain part of the environment (Figure 1). If MAS can solve the problem, the agent has to have knowledge and control over the entire environment. To do this, the agents are organized into a structure, in which they can interact with each other. Interactions between structures and agents are supposed to bring them benefits. Each agent has its preferences for the state, in which environment it should be (this is its goal). To describe this preference, the concept of utility ν was introduced, which causes the state of alignment of the environment Ω due to the agent's preferences.

$$\nu : \Omega \rightarrow \Re \qquad (10)$$

The environment that corresponds to preferences of the agent will have greater utility value (in other words: the agent will "feel better").

V. Matrix description of the multi-agent system

The paper key objective is to propose a modeling glucose-insulin paradigm in the form of MAS starting with a mathematical description and finishing the implementation of the program. This solution shows how we can implement features of agents for both the macro and micro processes in homeostasis of glycemia. Moreover, at the same time, we can allow operating on two scales: organs and cells scale. This approach results in a new quality of information. To describe the multi-agent system, the authors used the approach describing compartment modeling and using the rationality of graph theory. This approach simplifies the interpretation of what is happening in the multi-agent system, therefore, the behaviors of individual agents and their influence on other agents can be easily identified in the considered system.

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The analysis of MAS is a difficult task to implement due to the existence of the asynchronous relationships between agents occurring in the system. Additionally, each agent, which takes an active part in MAS has at least two behaviors: the first one is to receive incoming messages from other agents, and the other one is used by it to send the information to the chosen agent. By verification of the model, one can understand two aspects. The first one concerns information about the acceptable range of internal parameters of the model, which guarantees the stability of the model for the incoming information/extortion from outside. The second aspect concerns the range of input set, which ensures the correct stability and expected representation of the behavior of the modeled system.

We propose to describe MAS by using a comparison of network connections between the agents with the connections between vertices forming a graph. Nomenclature of the vertices is extended by the occurrence of behaviors that identifies the agent's behavior. In this perspective of the problem, the graph, which describes the interactions between agents with their associated behaviors is obtained. The assumptions are:

- Behaviors implemented in a given agent create a set of behaviors for the agent, which is a subset of behaviors occurring in the multi-agent system:

$$\sum A \in \Phi \tag{11}$$

$$\Phi \subseteq \Omega \tag{12}$$

  where:
  A - represents some behavior of an agent, Φ - represents a set of behaviors of a given agent, Ω - represents a set of behaviors of a multi-agent system.
- Agents who present the same behaviors are not identical with each other. It causes independent actions in the terms of time and each agent using the same behavior performs them in various time slots.
- Graph A=(V,E); |V|=n, |E|=m represents MAS basing on the assumption that:
  - n: number of graph vertices (number of agents),
  - m : number of behaviors appearing in MAS.
- Adjacency matrix $K \in M(n \times n;N)$ is defined in such a way that value in *i*-th line and in *j*-th column equals:
  - 0: if there is no communication between agents (no connection),
  - 1: if there is communication between agents (connection).

  Whereby:
  - k_{ii} represents the cyclical route of agent *i*-th,
  - k_{ij} represents the route from agent *i*-th to agent *j*-th.
- The sum of the same behaviors is one behavior:

$$\sum_i A_{1i} = A_1 \tag{13}$$

- Behavioral matrix $A \in M(n \times n; B)$ (where B designates the set of behaviors within the scope of the multi-agent system) is defined in such a way that a value in i-th line corresponds to behavior responsible for communication between agent *i*-th and agent *j*-th, whereby:
  - Behavior A_{ii} represents internal behavior (cyclical) of agent *i*-th,
  - Behavior A_{ij} represents information exchange from agent *i*-th to agent *j*-th.

Taking the above assumptions into consideration, it is possible to describe MAS with the use of matrix equation:

$$A^T K + D = \Phi \tag{14}$$

where:
A^T is the transpose of a matrix of agents' behaviors; K is a matrix of connections between agents; D is a matrix of agents' internal behaviors; Φ is a matrix representing the multi-agent system.

Analysis of the above equation will be presented on examples of multi-agent system. Both examples will rely on a different number of behaviors occurring in the multi-agent system.

VI. Examples

In this paragraph, authors demonstrate examples of the use of a matrix to describe MAS and to select unknown behavior.

A. The example of two-agent description based on the matrix representation

Let us consider the multi-agent system, where two agents A1 and A2 have predefined behaviors, and A11 and A22 are internal behaviors and A12 and A21 are external behaviors (Figure 6).

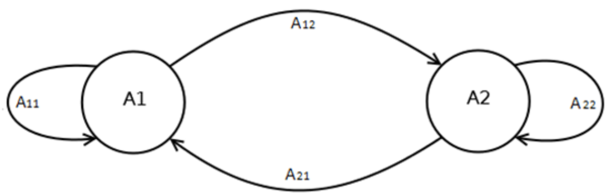

Figure 6. Two-agent system.

For the following example, adequate matrixes will be defined:

$$A = \begin{bmatrix} A_{21} - A_{12} & A_{12} \\ A_{21} & A_{12} - A_{21} \end{bmatrix} \quad (15)$$

$$A^T = \begin{bmatrix} A_{21} - A_{12} & A_{21} \\ A_{12} & A_{12} - A_{21} \end{bmatrix} \quad (16)$$

$$K = \begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix} \quad (17)$$

$$D = \begin{bmatrix} A_{11} & 0 \\ 0 & A_{22} \end{bmatrix} \quad (18)$$

Substituting to equation (15) we obtain a representation of MAS in the form of:

$$[\Phi] = \begin{bmatrix} A_{11} + A_{21} & A_{21} - A_{12} \\ A_{12} - A_{21} & A_{22} + A_{12} \end{bmatrix} \quad (19)$$

Conducting a detailed analysis of the matrix Φ we receive information about:

- First minor (φ_1) of a matrix Φ represents internal and incoming behaviors to agent $A_{1:}$

$$\varphi_1 = A_{11} + A_{21} \quad (20)$$

- Second minor (φ_2) of a matrix Φ represents behaviors of data exchange between agents A_1 and $A_{2:}$

$$\varphi_2 = A_{21} - A_{12} \quad (21)$$

- Third minor (φ_3) of a matrix Φ represents data exchange between agents A_1 and $A_{2:}$

$$\varphi_3 = A_{12} - A_{21} \quad (13)$$

- Fourth minor (φ_4) of a matrix Φ represents internal and incoming behaviors to agent $A_{2:}$

$$\varphi_4 = A_{22} + A_{12} \quad (22)$$

- Trace of a matrix represents behaviors occurring in the multi-agent system:

$$Tr[\Phi] = A_{11} + A_{21} + A_{22} + A_{12} \quad (23)$$

The examples were designed to show the application of (14) to describe MAS and the equivalence with the use of a graph. Description using matrixes is helpful in such a way that, in a compact form, it contains a representation of the dynamics of the multi-agent system. It is not relevant what type of behaviors are written using matrix A. That is why the authors consider this record as universal. The results matrix Φ contains much information, from which one can restore the functioning of the multi-agent system, basing solely on the content of individual cells of the matrix. Individual cells φ_i make it possible to obtain information on what types of behavior are present in the agent - whether they are its own internal behaviors (e.g., A_{11}) or behaviors associated with taking or receiving information to/from another agent (e.g., A_{21}). Additionally, the sum of the behavior of a given line (e.g., $\varphi_1 + \varphi_2$) is interpreted as the behavior occurring in the agent (e.g., for A_1). The results matrix can also determine whether, in the multi-agent system, there is at least one bidirectional communication between agents. To verify whether in MAS the exchange of information occurs, it is necessary to check whether the following identity is met:

$$Tr[\Phi] = \sum_i \varphi_i \quad (24)$$

To verify the above relationship, the examples discussed earlier can be used:

$$A_{11} + A_{21} + A_{22} + A_{12} = A_{11} + A_{21} + A_{22} + A_{12} \Leftrightarrow Tr[\Phi] = \sum_i \varphi_i \quad (25)$$

B. The example of matrix representation for identification of desired behavior

The experiment is quite specific. This uniqueness is based on the use of the matrix record, introduced in Section III, to determine unknown behavior in the multi-agent system. The experiment was based on a two-agent representation of the glucose homeostasis system. The first agent represents the entire mechanism of normoglycemia in the case of type 1 diabetic patient. The second agent represents insulin delivery in the form of external administration (Figure 7). The purpose of this experiment is to define the behavior responsible for sending "information" from Agent A1 to Agent A2 so that the dose of insulin delivered contributes to the metabolism of glucose.

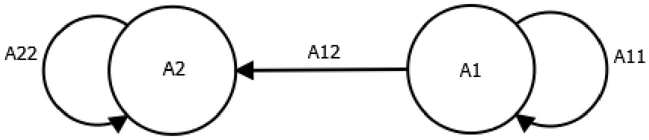

Figure 7. Diagram of MAS for the experiment.

Based on the concepts introduced in the section above, we can define the appropriate arrays, and so the matrix A:

$$A = \begin{bmatrix} -A_{12} & A_{12} \\ 0 & A_{12} \end{bmatrix} \qquad (26)$$

matrix K:

$$K = \begin{bmatrix} 0 & 1 \\ 0 & 0 \end{bmatrix} \qquad (27)$$

matrix D:

$$D = \begin{bmatrix} A_{11} & 0 \\ 0 & A_{22} \end{bmatrix} \qquad (28)$$

The matrix of MAS is defined by the corresponding relation between the previously mentioned matrices so that the system matrix is:

$$\Phi = \begin{bmatrix} A_{11} & -A_{12} \\ 0 & A_{22} + A_{12} \end{bmatrix} \qquad (29)$$

The trace of the matrix:

$$Tr\phi = A_{22} + A_{11} + A_{12} \qquad (30)$$

In this particular case, the meaning of the individual behavior is as follows:

- Behavior A_{11} is responsible for the insulin production that will eventually be introduced into the system. This behavior may also represent a buffer that stores a certain amount of insulin.
- Behavior A_{22} represents all the phenomena occurring in the glycemic homeostasis system, along with the ways of insulin utilization.
- Behavior A_{12} is responsible for the exchange of information (from agent A1 to agent A2) - this behavior should be determined.

The purpose here is to define the behavior A12 in such a way as to ensure insulin levels of φ_{A2}=7 [uIU/ml] for Agent A2. Below, a procedure to achieve our goal is presented:

1. Simulation for the conditions specified for a person with type 1 diabetes (without insulin infusion) (Figure 10).

2. Transform the pattern (22) into a form that allows us to calculate the desired behavior. In this case, we get:

$$A_{12} = \varphi_{A2} - A_{22} \qquad (31)$$

3. Perform curve fitting procedure (Figure 14) to the points obtained. This procedure was performed in MATLAB environment using the "fctool" command. The fit was done using a linear function. The following form of function is given:

$$f(A_{12}) = -0{,}0914t + 6{,}14 \qquad (32)$$

4. The last step was to implement the equation described in (24) into the body of the insulin dispensing agent. The simulation was started and a comparative analysis of data from the insulin-free model and from the model, in which the found behavior A_{12}.

Below are the following drawings corresponding to the mentioned above points.

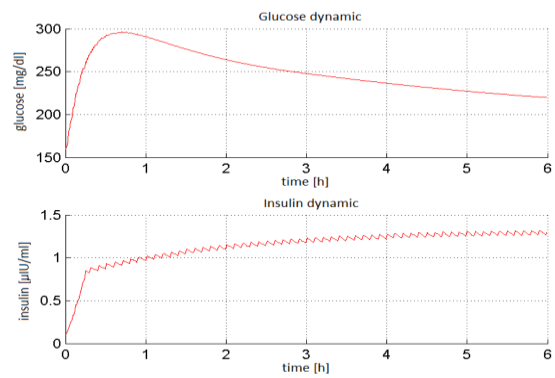

Figure 8. Simulation result for a person with type 1 diabetes - without insulin.

As can be deduced from Figure 10, the concept of using a matrix description to identify unknown behaviors is the most appropriate approach.

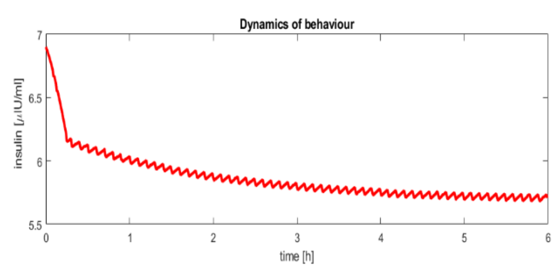

Figure 9. Chart for variability of behavior A_{12}.

Using (22), it is possible to select unknown behavior in such a way that the preset value can be maintained throughout the system under consideration. By focusing on the selected part of matrix φ, there is an opportunity to declare such an unknown behavior that will result each value from the agent the minor describes. This is the second case presented in this experiment. As a result of matching A_{12}, it has become possible to maintain insulin levels of 7 [µIU/ml] by the agent A2.

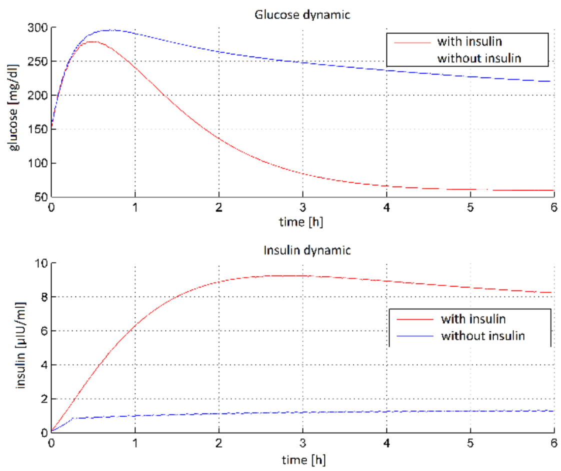

Figure 10. Simulation results for two cases: without insulin (blue curve), including the behavior of insulin dosing into the multiple agent system (red curve).

Of course, the quality of the curve fitting to the measurement points (Figure 8 and 9) directly affects the quality of the results generated by the multi-agent system.

VII. CONCLUSIONS

In this paper, we consider the problem of investigation of the complex biological system using compartment, fuzzy and multi-agent approaches.

We performed the analysis of MAS with the use of graph theory and matrix calculus. This approach can help us analyze the operation of such system in two ways: quantitative and qualitative ones. The use of matrix record enables performance of analysis of the internal multi-agent system involving the assignment of behaviors to particular agents. External analysis of MAS with the use of introduced record allows the description of the relation between agents and selection of such unknown behavior of an agent, which will meet the intended purpose or criterion implemented by the multi-agent system. In the second example, it is shown how using matrix equation allows finding the desired behavior of multi-agent system. For the general case, in which the agents (and the multi-agent system) process several volumes, each of these factors must be represented by a separate graph of accurate dependency. Generally speaking, each value can represent a different graph of connections between agents, and agents can have different numbers and behaviors intended to process these values. Matrix equation (15) proposed by authors, will be the subject of further work towards stability study of the multi-agent system.

REFERENCES

[1] S. Meszyński, and O. Sokolov, "Modeling of Complex Multiagent Behavior Using Matrix Representation," INTELLI 2017, The Sixth International Conference on Intelligent Systems and Applications, pp.32-37, July 23-27, 2017 - Nice, France, https://www.iaria.org/conferences2017/ProgramINTELLI17.html.

[2] P. Agre, "Computational theories of interaction and agency," Mit Press, 1996.

[3] F. Bellifemine, A. Poggi, and G. Rimassa, "Developing multi-agent systems with JADE," International Workshop on Agent Theories, Architectures, and Languages, Springer Berlin Heidelberg, 2000.

[4] W. J. Bosl, "Systems biology by the rules: hybrid intelligent systems for pathway modeling and discovery," BMC systems biology, 1(1):13, 2007.

[5] C. Cobelli, G. Toffolo, and E. Ferrannini, "A model of glucose kinetics and their control by insulin, compartmental and noncompartmental approaches," Mathematical biosciences, 72(2):291–315, 1984.

[6] A. Helleboogh, G. Vizzari, A. Uhrmacher, and F. Michel, "Modeling dynamic environments in multi-agent simulation," Autonomous Agents and Multi-Agent Systems 14.1: 87-116, 2007.

[7] H. S. Nwana, "Software agents: an overview," The Knowledge Engineering Review, 1996, 11(3), pp. 205–244. doi: 10.1017/S026988890000789X.

[8] R. S. Parker and F. J. Doyle, "Control-relevant modeling in drug delivery," Advanced drug delivery reviews, 48(2):211–228, 2001.

[9] S. Parson and M. Wooldridge, "Game Theory and Decision Theory in Multi-Agent Systems," Kluwer Academic Publisher, 2000.

[10] T. Seth and U. Wilensky, "NetLogo: Design and implementation of a multi-agent modeling environment," Proceedings of agent, vol. 2004.

[11] S. Soylu, K. Danişman, I.E. Saçu, and M. Alçi, "Closed-loop control of blood glucose level in type-1 diabetics: A simulation study," Electrical and Electronics Engineering (ELECO), 2013 8th International Conference on. IEEE, 2013.

[12] P. Stone and M. Veloso, "Multiagent systems: A survey from a machine learning perspective," Autonomous Robots 8.3: pp. 345-383, 2000.

[13] G. Toffolo, R.N. Bergman, D.T. Finegood, C. R. Bowden, and C. Cobelli, "Quantitative estimation of beta cell sensitivity to glucose in the intact organism: a minimal model of insulin kinetics in the dog," Diabetes, 29(12):979–990, 1980.

[14] P. J. Wangerman and F. R. Stengel, "Optimization and Coordination of Multiagent Systems Using Principled Negotiation," Journal of guidance, control, and dynamics, vol. 22, No. 1, 1999.

[15] M. Wooldridge, "An introduction to multiagent systems," John Wiley& Sons, 2009.