# The human body metabolism process mathematical simulation based on Lotka-Volterra model

Andriy Oliynyk*[a], Eugene Oliynyk[b], Olexandr Pyptiuk[c], Róża Dzierżak[d], Małgorzata Szatkowska[d], Svetlana Uvaysova[e], Ainur Kozbekova[f]

[a]Ivano-Frankivsk National Technical University of Oil and Gas; [b]Vasyl Stephanyk Precarpathian National University; [c]Ivano-Frankivsk National Medical University; [d]Lublin University of Technology, Nadbystrzycka 38 D, 20-618 Lublin, Poland; [e]National Research University Higher School of Economics; [f]Institute of Information and Computational Technologies, Almaty, Kazakhstan

## ABSTRACT

The mathematical model of metabolism process in human organism based on Lotka-Volterra model has beeng proposed, considering healing regime, nutrition system, features of insulin and sugar fragmentation process in the organism. The numerical algorithm of the model using IV-order Runge-Kutta method has been realized. After the result of calculations the conclusions have been made, recommendations about using the modeling results have been showed, the vectors of the following researches are defined.

**Keywords:** Lotka-Volterra model, metabolism, Runge-Kutta method, fragmentation process, insulin, diabetes.

## 1. INTRODUCTION

The problems of the human body metabolism process modeling was researched by the large number of authors [1-3], in particular, the generalized model of diabetes was created [1] that gives an opportunity to find out the sugar level in the organism that suffers from the diabetes and requires the insulin injection. However, the given models usually using the discontinuous Heaviside or Dirac functions that makes their practical realization a lot harder. Besides, those models allow modeling of the metabolism only for the organisms that require injections (I-type diabetes) at the time, when significant amount of sick people suffer from II-type diabetes, when the medications are not injected, but taken by the patient orally, following the clearly defined schedule that is set by the specialist. The aim of research is creation and program realization of I-II types diabetes model for the blood insulin and sugar level evaluation considering the healing method, nutrition regime and its compound for used medication dose optimization [4-6],. For this purpose the model of biological species competition fighting for survival (predator-prey model), published in 1925 is being used. This model was proposed by two famous mathematicians – Alfred J. Lotka and Vito Volterra:

$$\begin{cases} \dfrac{dx}{dt} = k_1 x(t) - g_1 x(t) y(t) \\ \dfrac{dy}{dt} = -k_2 y(t) + g_2 x(t) y(t) \end{cases} \qquad (1)$$

$$x(0) = x_0, y(0) = y_0$$

where $x(t)$ - amount of the prey population, $y(t)$ - amount of the predator population, $k_i, g_i, i = 1,2$ - coefficients of the model.

The given model allows both to become analytic, exact solution and to realize it with numerical methods with introduction of the new components that are corresponding processes with using of model continuous functions.

*admin@nung.edu.ua

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For the guarantee of model correctness the uniqueness existence and stability of received results is researched. Also, the program complex with corresponding interface for the practical model realization in medical institution is being created.

## 2. METHOD

For the modeling of the diabetes metabolism process following functions are introduced: $x(t)$ – blood sugar level, $y(t)$- blood insulin level. Model (1) makes a transformation and can be presented in the following outlook [7]:

$$\begin{cases} \dfrac{dy}{dt} = -k_1 y(t) + k_2 w(t) \\ \dfrac{dx}{dt} = -k_3 x(t) y(t) + k_4 z(t) \end{cases} \tag{2}$$

with the initial conditions:

$$\begin{aligned} y(0) &= y_0, \\ x(0) &= x_0, \end{aligned} \tag{3}$$

that are setting the initial blood sugar and insulin level. The main feature of this model is introduction of additional functions $w(t)$ and $z(t)$ in the system (1), whose meaning will be explained below. Context of the equations in the system (2) can be presented like that: the amount of insulin in the organism is decreasing per unit time pro rata to its initial concentration, however it can be regulated by insulin injections or inner intake of corresponding less intensive medications; the amount of sugar in the organism is decreasing because of its present insulin neutralization and is increasing because of presence of sugar in food, which is taken by the patient [8].

The function $w(t)$ defines the insulin injective imposition regime or medications intake, it gives an opportunity to model the amount of the imposed insulin and has a parametric outlook:

$$w(t) = \sum_{i=1}^{k} \frac{b_i}{m_i (t - t_i)^2 + 1}, \tag{4}$$

where $t_i$ - moments of insulin imposition or medications intake, $b_i$ - dose of the medication, k - number of the medications intake during the day, $m_i$ - empirical coefficient that depends on the way of medication imposition in the organism (during the injective way of the intake its value is higher than inner intake indication). The peculiarity of $w(t)$ modeling is the fact that it describes the process numerically and quantitative – it has just as many maximums as the quantity of injections or medications inner intake and due its help –makes possible the regulation and modeling of insulin digestion.

Describing in the same axes the plot of $w(t)$ during the injective and inner intake of insulin (fig.1) , the following quantitative characteristics of the process can be obtained:

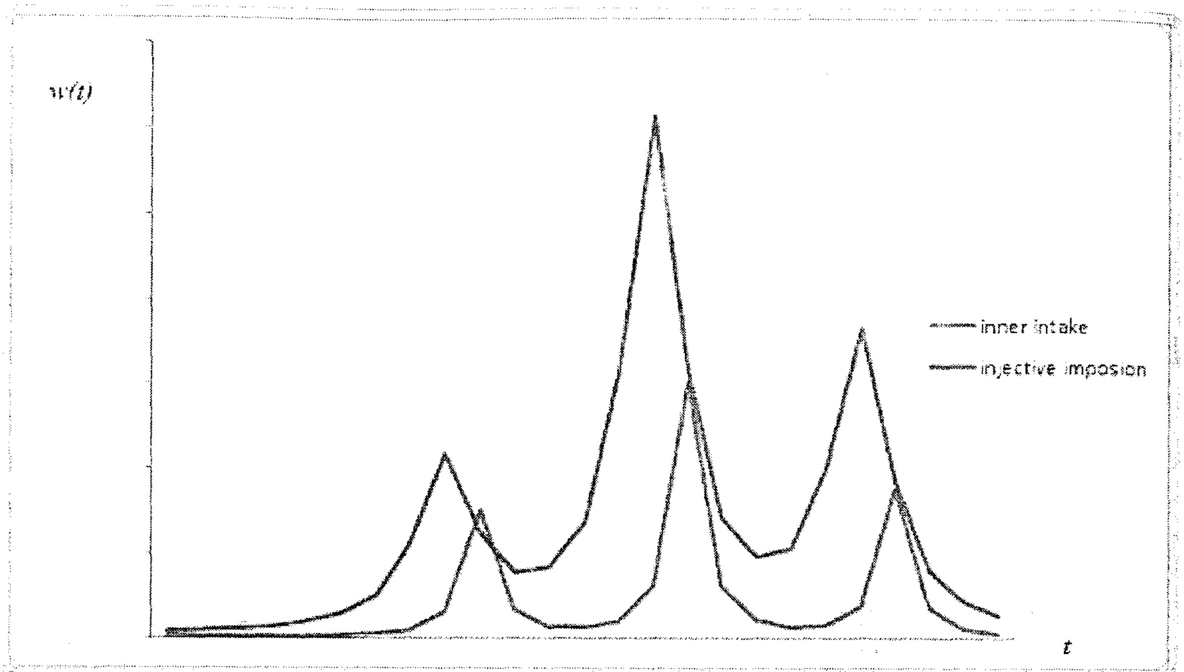


Figure 1. Plot of insulin level in the human body depending on the medications intake way

Function $z(t)$ defines sugar imposition regime (with food), it allows to model the quantity of imposed sugar and meal time (breakfast, dinner, supper, night snack etc.) and has analytically corresponding outlook to the formula (4):

$$z(t) = \sum_{i=1}^{n} \frac{c_j}{n_i (t - t_j)^2 + 1}, \tag{5}$$

where $t_i$ - moments of food intake, $c_i$ - sugar dose that goes into the human body during the food intake, $n_i$ - coefficient that models the level of sugar absorption in the human organism, n – quantity of meal intakes. The way of setting $z(t)$ and $w(t)$ is unique, it is proposed to use them, for their stability and calculation accuracy during the modeling, instead of discontinuous functions, functions with Gaussian distribution and piecewise linear approximation of $w(t)$ function [9]. In some distinct cases, when the symmetry of $w(t)$ plot apropos straight lines $t = t_1^*$ doesn't correspond to the real picture of the modeling process, the way of presentation (4) can be modified in the following outlook:

$$w(t) = \sum_{i=1}^{k} g_i(t), \tag{6}$$

where $g_i(t)$ can be presented as:

$$g_i(t) = \begin{cases} \dfrac{b_i}{m_i (t - t_i^*)^2 + 1}, t \le t_i^* \\ \dfrac{b_i}{\widetilde{m}_i (t - t_i^*)^2 + 1}, t > t_i^* \end{cases} \tag{7}$$

where $t_i^*$ - moment of maximal influence of the medication, $m_i$ - coefficient that has same meaning as in (4), $\widetilde{m}_i$ - coefficient that models the level of medication influence fading. In the common case $m_i \neq \widetilde{m}_i$, but this condition doesn't break the continuity of both function $g_i(t)$ and its derivative $g_i'(t)$ in the $t = t^*$ point. It's obvious that:

$$g_i(t_1^* - 0) = g_i(t_1^* + 0), \tag{8}$$

that comes directly from (7), besides:

$$g_i'(t_1^* - 0) = g_i'(t_1^* + 0) = 0, \tag{9}$$

because for:

$$f(t) = \frac{b_i}{m_i(t - t_i^*)^2 + 1}; \; h(t) = \frac{b_i}{\widetilde{m}_i(t - t_i^*)^2 + 1} \tag{10}$$

the values of the derivatives

$$f'(t) = -\frac{2b_i(t - t_i^*)m_i}{\left[m_i(t - t_i^*)^2 + 1\right]^2}, \tag{11}$$

$$h'(t) = -\frac{2b_i(t - t_i^*)\widetilde{m}_i}{\left[\widetilde{m}_i(t - t_i^*)^2 + 1\right]^2}. \tag{12}$$

in the $t = t^*$ point are equal and have a value of zero, thus the condition of continuity (9) is implemented.

Conditions and correlations (8)-(12) are setting the continuity of $g_i(t)$ and $g_i'(t)$ in the $t = t^*$ point that also facilitates both model adequacy and the stability of calculations.

## 3. SYSTEM RESEARCH AND RESULT GENERALIZATION

If the human doesn't suffer from diabetes, in this case system (2) is characterized with coefficients $k_1, k_2, k_3, k_4 \le 1$, that fits to this case. Thus, when $k_1 = k_2 = k_3 = k_4 = 0$, system (2) with conditions (3) is solved analytically and the solution can be represented like:

$$\begin{aligned} y(t) &= y_0 \\ x(t) &= x_0 \end{aligned} \tag{13}$$

and that is trivial and confirms the stability of blood sugar and insulin level. The solution of the system (2) with the conditions $k_1, k_2, k_3, k_4 \le 1$ differs not so much from (13) due to the ODE system solution stability [10]. In the common case, system (2) doesn't integrate accurately, thus the IV-order Runge-Kutta method is used for its solution and the corresponding software is created. For the calculation following numeric characteristics are implemented:

- coefficient that characterizes the level of insulin fragmentation $(k_1)$;
- coefficient that characterizes the level of injective insulin absorption ($k_2$);
- coefficient of sugar abolition due to insulin $(k_3)$;
- coefficient of absorption of sugar, that comes with food $(k_4)$;
- numeric value of insulin dose that is imposed into the organism $b_i, i = \overline{1,k}$, where $k$ – amount of the insulin injections during the day;
- moments of insulin imposition ($t_i$);
- coefficients that characterize the time of injection effect $m_i, i = \overline{1,k}$;
- numeric value of sugar amount in food $c_j, j = \overline{1,n}$, where $n$ – amount of the meal intakes;
- moments of meal intake ($t_j$);
- level of sugar absorption that comes with food ($n_j$);
- The step of calculation is taken equal 0.1, all the numerical results are considered during one day (24 hours).

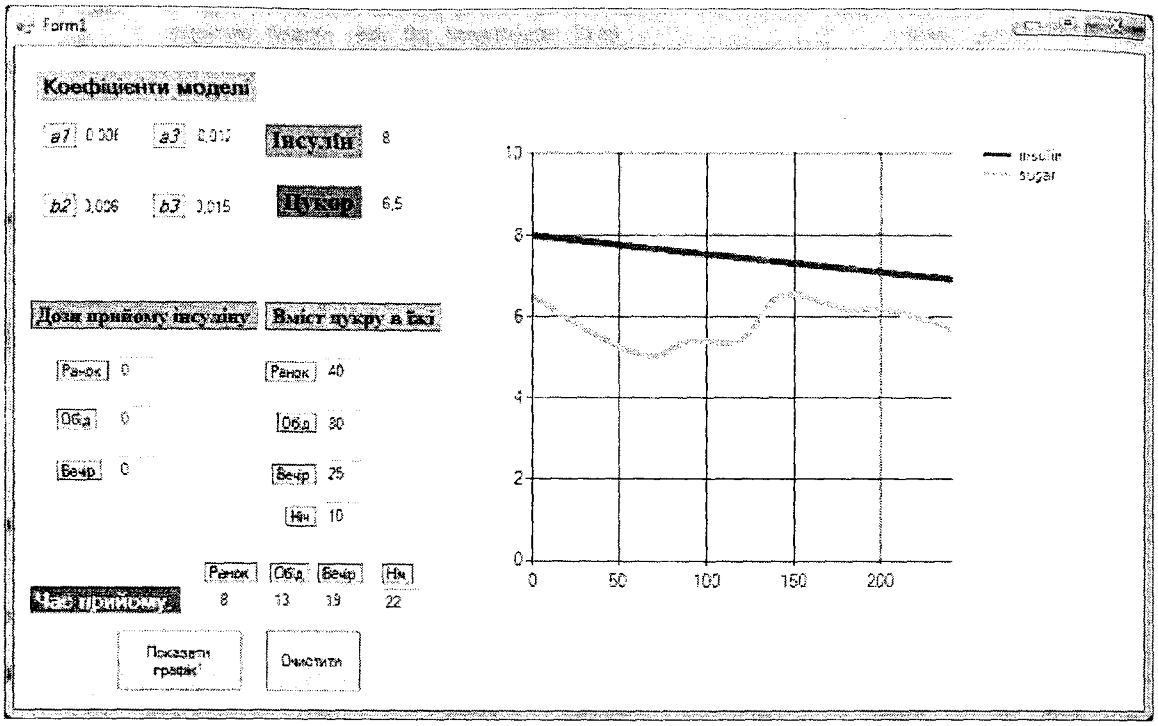


Figure 2. The program interface to the insulin and sugar level calculation (rational everyday meal regime).

In the numerical algorithm realization process such functions are found that demonstrate the change of insulin level (blue line) and sugar level (yellow line) during the day. The pict.2 shows the common outlook of the program interface.

The coefficients have the following variation:

$$5 \le y_0 \le 10, \quad 5 \le x_0 \le 7, \quad 0 \le b_1 \le 4, \quad 0 \le b_2 \le 12, \quad 0 \le b_3 \le 8,$$

$$0 \le k_1 \le 0.02,\ 0 \le c_1 \le 50, \quad 0 \le k_2 \le 0.05,\ 0 \le c_2 \le 150, \quad 0 \le k_3 \le 0.05,\ 0 \le c_3 \le 40, \quad 0 \le k_4 \le 0.04,\ 0 \le c_4 \le 10,$$

After the results of the calculations, the conclusion can be made:

- model allows to describe the variance of blood sugar level in the organism that suffers from diabetes in injective and in inner intake way (pills), depending on the features of the human body (coefficients $k_1$ and $k_3$) ,nutrition regime and medications, caloricity, sugar presence in food, dose of the medications. It's defined that values of $k_1 \in [0;0.001]; k_3 \in [0;0.002]; k_2 = 0; k_4 \in [0;0.001];$ are corresponding to the healthy organism, when blood sugar level is located in the permissible limits;
- when the values of coefficients( $k_1$ and $k_3$) are overreaching the given values, the blood insulin level is quickly decreasing and, respectively, blood sugar level is increasing and that requires medical treatment ( $k_2 \ne 0$ );
- with the fixed values of $k_1$ and $k_3$ it is researched how the blood sugar level depends on the insulin dose that goes in the organism during the treatment, the limits of those dose are defined and they allow to keep the blood sugar level in permissible limits;
- with the fixed dose of medications it is found how the nutrition regime and sugar presence in food make influence on the blood sugar level, the algorithm of optimization is proposed for the medication dose in case of corresponding diet compliance;

- the values of coefficients $k_2$ and $k_4$ are found, during which the insulin fragmentation process is happening so intensive that it may require more its additional imposition in the organism; in the simplest case the equations of insulin and sugar fragmentation can be presented like ( $k_2 = k_4$ ):

$$\begin{cases} y = y_0 e^{-k_1 t} \\ x = x_0 e^{y_0 \frac{k_3}{k_1}(e^{-k_1 t} - 1)} \end{cases} \quad . \tag{14}$$

The dependency (14) allows to set such levels of $k_1$ and $k_3$ during which the change of $x(t)$ and $y(t)$ takes place in permissible limits. Those conclusions will be fair also for the system (2) in case of $k_2, k_4 \leq 1$;

- the model (2) can be used for the recommendations about the nutrition regime of healthy people with the aim of stabilization of blood sugar level – it is showed that for the stable sugar level in the organism during the day breakfast and dinner should have more food with sugar presence in it, and supper should be less saturated with sugar (so as the night snack). Such situation is presented on figure 2 - the consisting of the sugar in the meal is presented in the corresponding column, the injection of insulin is on the zero level, if the meal regime is not rational and the person receive the main part of sugar in the afternoon and evening period – it can lead to the sugar level increasing (fig. 3), if such situation will have tendency to repeating during long time the risk of diabetes problems appearance can increase;

- the presented interface of model's shows the metabolism process during one day, but the model (2) can be adapted for the investigation of metabolism process during more longer period – a few months or years. In such cause the step of finite differences scheme of the IV-order method depends on the needing level of accuracy and stability of the results.

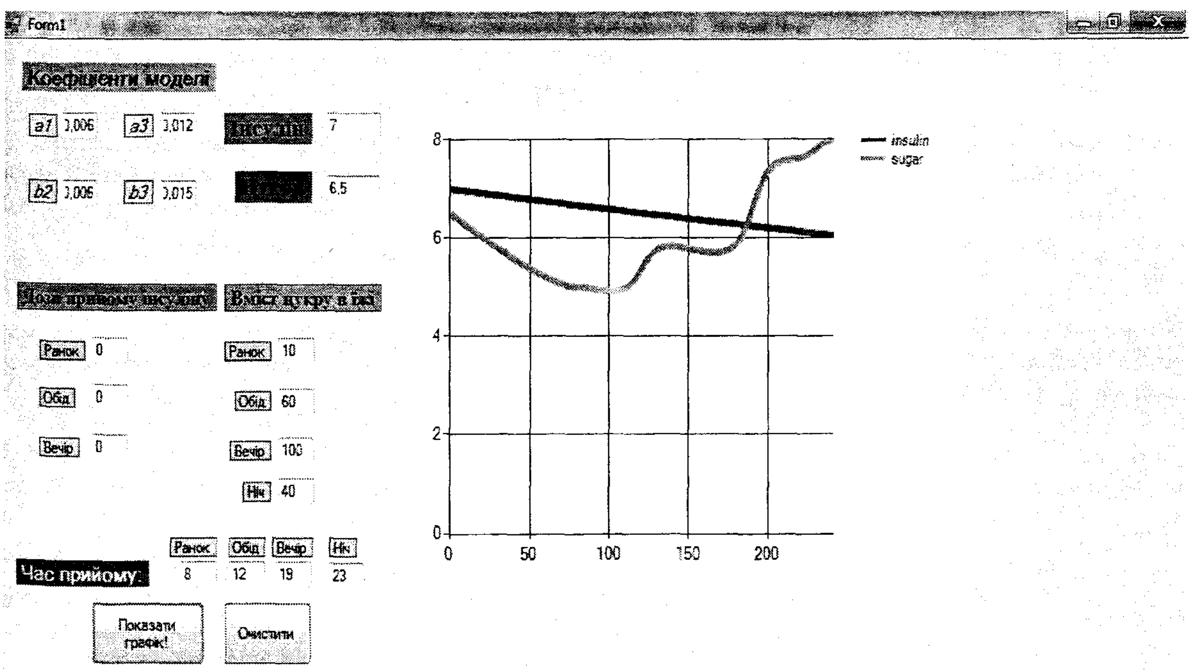


Figure 3. The sugar level increasing as result of irrational everyday meal regime.

## 4. CONCLUSIONS

The working on the methodology of defining the model coefficients on the basis of statistical data, which can be taken from corresponding medical institutions – from the mathematical point of view it would be interesting to put and to solve the coefficient inverse problem, which can allow to estimate the model's (2) coefficients using the results of blood tests in the clinical conditions – in such way it is possible to receive the data of x(t) and y(t) functions using the interpolation and approximation (the least squares method) procedures.

The research on the program complex from the side of providing its stable work, setting of the working data measures that don't cause the deprivation of numerical algorithm stability or becoming of invalid results thaient t are contrary to the real physical, mathematical and clinical picture of the process.

Development of the software that is adapted for the usage in the medical institutions.

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