Nonlinear Analysis: Modelling and Control, 2010, Vol. 15, No. 2, 213–232

Modelling of glycaemia dynamics: impact of physical exercises

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Received: 2009-10-06 **Revised:** 2010-04-26 **Published online:** 2010-06-01

Abstract. In this article the authors performed linear, nonlinear and numerical analysis of glycemic regulation mathematical model described by two differential equations with one delay argument. The results obtained in the linear analysis were used in numeric analysis while constructing stable periodic solutions applying the Runge–Kuto IV successive method in normal and diabetes cases. Impact of physical exercise on the dynamics of glucose and insulin was modelled as well while introducing two external periodical functions defining diet and physical exercise into the above mentioned model. We applied the simulation modelling program "Model Maker" for modelling.

Keywords: glycemic regulation, mathematical modeling of glycemic regulation, exercise and diabetes, impact of physical exercise to the control of glycemia.

1 Introduction

Physical exercise is an important factor in diabetes management. Physical exercise of diverse forms gives diverse results of glycemia. Although physical activity may be sometimes a risky method to loose weight while being ill with type 2 diabetes, regular exercises are the basis in diabetes treatment.

Appropriately selected physical activity increases the sensibility of cells to insulin, enhances the homeostasis of glucose and helps to reduce medicine doses. [1]. During exercising the uptake of glucoses to muscles increases proportionally to the intensity and duration of physical load. Exercises both stimulate glucose uptake independently from insulin stimulation and neutralise cell immunity to insulin [2].

While evaluating the type, duration and intensity of physical exercises it is necessary to consider the level of physical state of patients. Diabetics perform aerobical and anaerobical exercises. Anaerobical exercises last less than 2 minutes, for example short distance running, swimming or weight lifting. In this case namely cells receive ATP energy from sebum and carbohydrates from glycogen that accumulates in muscles. Aerobiocal exercises last over 2 minutes, for example, long distance running and other sporting fields.

The consequence of frequent intervals between intensive activity, i.e. interval between rapid warm-up exercises and heavy training, is a prominent glycogen consumption in muscles that highly increases insulin sensibility after active activity. During the period of long lasting active activity glucoses in blood drops down significantly and the resources of glycogen in muscles exhaust rather considerably. In case the activity is not coordinated with insulin doses the volume of glycogen in muscles during active activity is consumed faster than its resources are accumulated, therefore hypoglycemia may develop. When active activity lasts for a short period of time and is very intensive than the replenishing of human body with carbohydrates is the only efficient way to maintain the normal level of glycaemia. [3].

This theme are widely analyzed in the works of the world scientists see [4–18] and this fact proves that this theme is very significant in the sphere of medicine as the increasing number of patients become ill with diabetes mellitus annually.

We will analyse in this article mathematical model (1)–(2) and demonstrate that introduction of diet and physical load into the mentioned model allows applying it successfully to optimisation of glycaemia control and diabetes treatment.The investigated model (1)–(2) comprises two differential equations with one delay [19].

$$\dot{I}(t) = r_I \left[\frac{G(t)}{K_G} - \frac{I(t-h)}{K_I} \right] I(t), \tag{1}$$

$$\dot{G}(t) = r_G \left[1 + c \left[1 - \frac{I(t)}{K_I} \right] - \frac{G(t)}{K_G} \right] G(t). \tag{2}$$

In this model $I(t)$ is the level of active insulin in blood at the time moment t, K_I is the average value of insulin in blood, h – the time necessary for the production of insulin in pancreas β-cells. $G(t)$ is the level of glucose in blood (glycemia), K_G is the average value of glucose in the blood. Glycemic self-regulatory relations are interpreted as in a "predator-victim" task, where the insulin is a "predator" and sugar is a "victim". r_I, r_G are positive values characterizing the linear rate of production of insulin and sugar concentration in blood-line growth, and c is a parameter, that regulates the feedback of glycemia in Švitra [19].

In order to reach diabetes treatment efficiency it is very important to apply an appropriate treatment strategy. Application of physical load is an important factor both for treatment of diabetics and for keeping of good condition of healthy people. This treatment strategy is widely applied in clinical treatment of patients ill with diabetes.

In this article we will numerical method modeled the dynamics of glycemia in case of normal and diabetic cases introducing in model (1)–(2) two external periodic functions defining the nutritional $g(t) = g(t + 24)$ [20] and exercise $f(t) = f(t + 24)$.

Here $f(t)$ – is a linear function describing the intensity of physical load in normal case and in case of diabetes and $g(t)$ is a linear function describing the nutritional regime [20]. We suggest to apply the above mentioned functions for modelling the dynamics of glycaemia and insulin in general diagram submitted in Fig. 1. This scheme allows to model the dynamics of glycemia and insulin in the period of 3-days in case of normal and diabetes, where it is possible to introduce $g(t) = 1, \ldots, 6$ times a day and exercise are

introduced $f(t) = 1, \ldots, 2$ times a day.

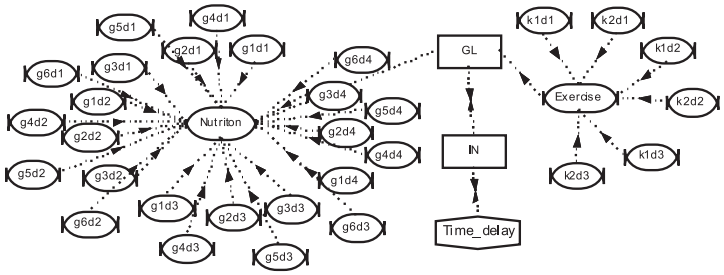

Fig. 1. The overall modeling scheme of glycemic regulation mathematical model (1)–(2) in normal and diabetic cases.

Before starting modeling exercise influence glycemic and insulin dynamics we will investigate in a qualitative way a model following the Bifurcation Theory [19] to determine model parameters.

2 Mathematical analysis

2.1 Linear analysis

We identified three positive equilibrium states of equations set (1)–(2):

$$I(t) \equiv G(t) \equiv 0, \tag{3}$$
$$I(t) \equiv 0, \quad G(t) \equiv (1+c)K_G, \tag{4}$$
$$I(t) \equiv K_I, \; G(t) \equiv K_G. \tag{5}$$

The result demonstrated that (3) and (4) the equilibrium states are unstable. We will investigate the stability of equilibrium state (5) after the following such changes of the variables:

$$I(t) = K_I\big[1 + x(t)\big] \quad \text{and} \quad G(t) = K_G\big[1 + y(t)\big]. \tag{6}$$

Then we replace equations system (1)–(2) by the following system of equations:

$$\dot{x}(t) = -r_I\big[x(t-h) - y(t)\big]\big[1 + x(t)\big], \tag{7}$$
$$\dot{y}(t) = -r_G\big[cx(t) + y(t)\big]\big[1 + y(t)\big]. \tag{8}$$

The characteristic quasipolinomial of the linear part of equation system (7)–(8) will be

$$P(\lambda) = \big(\lambda + r_I e^{-\lambda h}\big)(\lambda + r_G) + cr_G r_I = 0. \tag{9}$$

Theorem 1. *The solution of differential equations to be asymptotically stable, it is necessary and sufficient that all the roots of its characteristic equation should satisfy the inequality:*

$$\operatorname{Re}\lambda < 0.$$

This condition must be valid for all $P(\lambda)$ roots. Since it is rather difficult to calculate all quasipolinomial roots diverse negative characteristics of real parts of quasipolinomial roots of are of great importance. D-segmentation method is applied very often for investigation of quasipolinomial roots [19].

D-segmentation method

We will analyse the location of roots of characteristic quasipolinomial (9) in the plane of parameters r_I and C applying D-fragmentation method.

In this case our quasipolinomial (9) depends on three parameters

$$P(\lambda, r_I, c) = 0. \tag{10}$$

When equation (9) has a zero root $\lambda = 0$, then we get the lines $c = -1$ and $r_I = 0$.

When equation (9) has a purely imaginary roots $\lambda = i\sigma$, $\sigma > 0$, we receive the following curves (11)–(12) in parametric form, which we will draw in $r_I c$ plane

$$c = \frac{\sigma^2 - r_I(\sin(\sigma h) + r_G\cos(\sigma h))}{r_I r_G}, \tag{11}$$

$$r_I = \frac{\sigma r_G}{r_G\sin(\sigma h) - \sigma\cos(\sigma h)}, \tag{12}$$

where $\sigma \to 0$ then from the system of equations (11)–(12) we receive the following coordinates of reversible point

$$\lim_{\sigma\to 0} c = -1, \quad \lim_{\sigma\to 0} r_I \frac{1}{h - \frac{1}{r_G}}. \tag{13}$$

Then we will draw the above received parametric curves in D-segmentation plane and mark the return point coordinates in normal and diabetic cases.

While optimizing the values of parameters r_I and c both in a case of a healthy person and in the case of diabetics only positive values of these parameters have the meaning in glycemic modelling.

Applying "Maple" we charted D-segmentation curves in normal case with the following values of parameters $h = 6$, $K_I = 8$, $K_G = 100$, $r_G = 12$; in case of diabetes when the values of parameters are as follows $h = 5.8$, $K_I = 7$, $K_G = 125$, $r_G = 21.6$ [19].

In Fig. 2 and Fig. 3 we showed the asymptotic stability fields D_0 and D_2. We found that all real parts of equation roots in the field D_0 are negative. We also determined that during the transition from the field D_0 to the field D_2 we receive two roots, the real parts of which are positive. We determined that stable periodic solutions of the equation (1)–(2) in the field D_2.

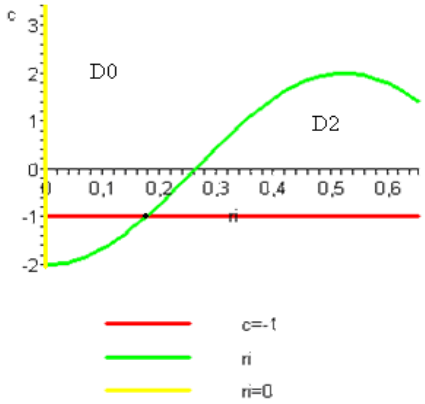

Fig. 2. D-segmentation curves in normal case.

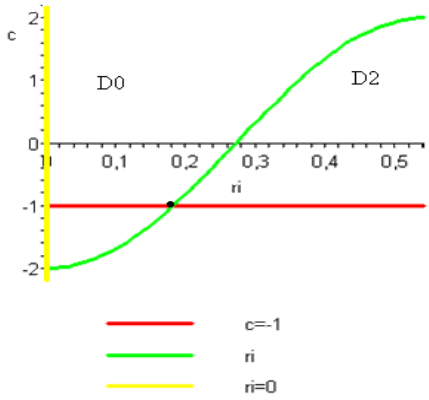

Fig. 3. D-segmentation curves in case of diabetes.

2.2 Nonlinear analysis

In this section we will construct the periodic solution of differential equation system (1)–(2) applying the theory of bifurcation provided by Švitra [19].

The system of equations (1)–(2) has been examined in the state of internal equilibrium $I(t) = K_I$ and in $G(t) = K_G$ environment. In this system of equations after the substitution of variables $I(t) = K_I[I + x(t)]$, $G(t) = K_G[I + y(t)]$ the following differential equations system was received:

$$\dot{x}(t) = -r_I\big[x(t-h) - y(t)\big]\big[1 + x(t)\big], \tag{14}$$

$$\dot{y}(t) = -r_G\big[cx(t) + y(t)\big]\big[1 + y(t)\big]. \tag{15}$$

The properties of Hutchinson equation suggest that in case of sufficiently small $\varepsilon = r_I - \frac{\pi}{2h}$ the equation (14) has a stable periodic solution

$$x(\tau) = \xi x_1(\tau) + \xi^2 x_2(\tau) + \cdots, \tag{16}$$

where

$$x_1(\tau) = \cos(\sigma_0\tau), \quad x_2(\tau) = \frac{1}{10}\big(\sin(2\sigma_0\tau) + \cos(2\sigma_0\tau)\big), \tag{17}$$

ε, τ in equations (16) and (17) are the following:

$$\xi = \sqrt{\frac{\eta_0'\varepsilon}{d_0}}, \quad \tau = \frac{t}{1 - (\frac{c_0\eta_0'}{d_0} + \frac{\omega_0'}{\sigma_0})\varepsilon}, \tag{18}$$

where σ_0, c_0, d_0 are expressed in formulas [19]:

$$\sigma_0 = \frac{\pi}{2h}, \quad c_0 = \frac{\pi + 6}{10(\pi^2 + 4)}, \quad d_0 = \frac{\sigma_0(3\pi - 2)}{10(\pi^2 + 4)}, \tag{19}$$

when τ_0', σ_0', η_0', ω_0' were expressed as

$$\tau_0' = \frac{2\pi}{\pi^2+4}, \quad \sigma_0' = \frac{4}{\pi^2+4}, \tag{20}$$

$$\eta_0' = \left[1 - \frac{\alpha_0 r_G^2}{\sigma_0^2 + r_G^2}\right]\tau_0' - \frac{\alpha_0 r_G \sigma_0}{\sigma_0^2 + r_G^2}\sigma_0', \tag{21}$$

$$\omega_0' = \frac{\alpha_0 r_G \sigma_0}{\sigma_0^2 + r_G^2}\tau_0' + \left[1 - \frac{\alpha_0 r_G^2}{\sigma_0^2 + r_G^2}\right]\sigma_0'. \tag{22}$$

Differential equation (15) also has a single stable periodic solution

$$y(\tau) = \xi y_1(\tau) + \xi^2 y_2(\tau) + \cdots . \tag{23}$$

After the appropriate standardization of time ratios of line (23) can be sought applying the method of uncertain coefficients. Then we get

$$\dot{y}_1(\tau) + r_G y_1(\tau) = -r_G c x_1(\tau), \tag{24}$$

$$\dot{y}_2(\tau) + r_G y_2(\tau) = -r_G c x_2(\tau) + \dot{y}_1(\tau) y_1(\tau). \tag{25}$$

We get that $y_1(\tau)$ in the equation (24) are as follows:

$$y_1(\tau) = -\frac{r_G c(\sigma_0 \sin(\sigma_0\tau) + r_G \cos(\sigma_0\tau))}{\sigma_0^2 + r_G^2} \tag{26}$$

From equation (25) we get, that

$$y_2(\tau) = A\sin(2\sigma_0\tau) + B\cos(2\sigma_0\tau), \tag{27}$$

where

$$A = \frac{1}{4\sigma_0^2 + r_G^2}[W_1 r_G - 2W_2\sigma_0], \tag{28}$$

$$B = \frac{1}{4\sigma_0^2 + r_G^2}[W_2 r_G - 2W_1\sigma_0]. \tag{29}$$

And that W_1, W_2will be the following:

$$W_1 = -\frac{r_G c}{10} + \frac{\sigma_0 c^2 r_G^2}{2(\sigma_0^2 + r_G^2)}\left[\sigma_0^2 - r_G^2\right], \tag{30}$$

$$W_2 = -\frac{r_G c}{5} + \frac{\sigma_0^2 c^2 r_G^3}{\sigma_0^2 + r_G^2}. \tag{31}$$

Consequently the differential equations (14)–(15) will have stable periodic solutions.

Theorem 2. *When* $0 < r_I - \frac{\pi}{2h} = \varepsilon \ll 1$, $r_I c = \alpha_0 \varepsilon$ *and* $\eta_0' > 0$, *the differential equation system* (14)–(15) *in the environment of a sufficiently small the equilibrium state of* $I(t) \equiv K_I$ *and* $G(t) \equiv K_G$ *have the only stable environment periodic solutions that at any time interval* ε^{-1} *are expressed in formulas.*

$$I(t) = K_I\big[1 + \xi\cos(\sigma_0\tau) + \xi^2 x_2(\tau) + O\big(\xi^3\big)\big], \tag{32}$$

$$G(t) = K_G\big[1 + \xi y_1(\tau) + \xi^2 y_2(\tau) + O\big(\xi^3\big)\big], \tag{33}$$

where functions $x_2(\tau)$, $y_1(\tau)$, $y_2(\tau)$ *are respectively expressed in formulas* (17), (26), (27), *and* ξ, τ, σ_0, *are defined by formulas* (18)–(19).

Applying formulas (14)–(33) we will construct approximate formulas of solution (32)–(33) in normal and diabetes cases. In normal cases approximate formulas will be:

$$\begin{aligned} I(t) \approx 8\Bigg[1 &+ 1,53473\cos(0,3438t) \\ &+ 2,3554\left(\frac{1}{10}\sin(0,6875t) + \frac{1}{5}\cos(0,6875t)\right)\Bigg], \end{aligned} \tag{34}$$

$$\begin{aligned} G(t) \approx 100\big[1 &+ 1,53473\big(0,0031\sin(0,3438t) + 0,1399\cos(0,3438t)\big) \\ &- 2,3554\big(0,0435\sin(0,6875t) + 0,0247\cos(0,6875t)\big)\big], \end{aligned} \tag{35}$$

when $r_I = 0.39$; $r_G = 12.00$; $c = 0.14$; $h = 6.00$; $\xi = 1.5347$; $\tau = 1.3131t$; $\sigma_0 = 0.2618$.

In diabetic cases approximate formulas will be:

$$\begin{aligned} I(t) \approx 7\Bigg[1 &+ 1,4158\cos(0,3394t) \\ &+ 2,0043\left(\frac{1}{10}\sin(0,6788t) + \frac{1}{5}\cos(0,6788t)\right)\Bigg], \end{aligned} \tag{36}$$

$$\begin{aligned} G(t) \approx 125\big[1 &- 1,4158\big(0,0018\sin(0,3394t) + 0,1399\cos(0,3394t)\big) \\ &- 2,0043\big(0,0719\sin(0,6788t) + 0,0248\cos(0,6788t)\big)\big], \end{aligned} \tag{37}$$

when $r_I = 0.39$; $r_G = 21.60$; $c = 0.14$; $h = 5.8$; $\xi = 1.4158$; $\tau = 1.2538t$; $\sigma_0 = 0.2708$.

2.3 Mathematical modelling of the impact of diet and physical exercise on the dynamics of glucoses and insulin

After execution of a qualitative analysis mathematical model (1)–(2) of glycemic regulation we will apply values optimized parameters while executing a numerical analysis.

We will try to find differential equation with the delay solutions describing glycemic and insulin dynamics using the Runge–Kuto IV sequence method.

We will chart the comparison of glucoses and insulin numerical solutions of differential equation system (1)–(2) in normal and diabetes cases with the experimental points,

respectively Fig. 4 and Fig. 5. Experimental points in normal case are taken from [21], and diabetes case are taken from [22]. In normal case we use the following values of parameters: $h = 6.00$; $K_I = 8.00$; $K_G = 100.00$; $r_G = 12.00$; $r_I = 0.39$; $c = 0.14$. While searching for a stable periodic numerical solution in case of diabetes we used the following parameters values: $h = 5.80$; $K_I = 7.00$; $K_G = 125.00$; $r_G = 21.60$; $r_I = 0.39$; $c = 0.14$.

In Figs. 6–7 we will show the GL numerical solutions of differential equation (1)–(2) system solutions received with the help of formula (1) and GLA solutions (dotted line) received with the help of periodical approximate formulas (35) and (37) in normal and diabetes cases respectively.

In Figs. 8–9 we will show the IN numerical solutions of differential equation (1)–(2) system solutions received with the help of formula (2) and LNA solutions (dotted line) received with the help of periodical approximate formulas (34) and (36) in normal and diabetes cases respectively.

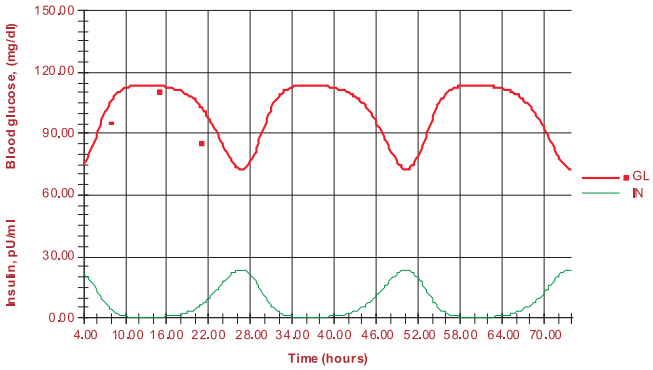

Fig. 4. Numerical solution of model (1)–(2) in normal case.

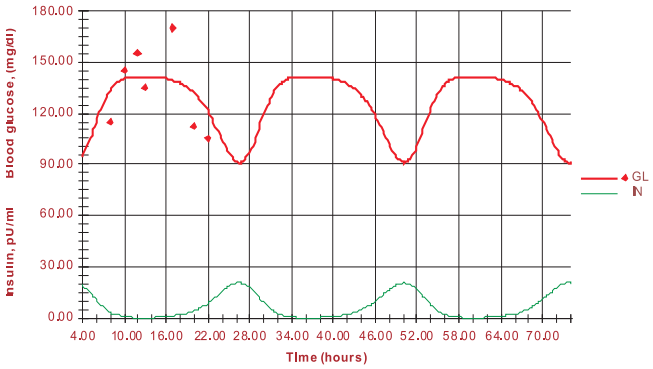

Fig. 5. Numerical solution of model (1)–(2) in diabetic case.

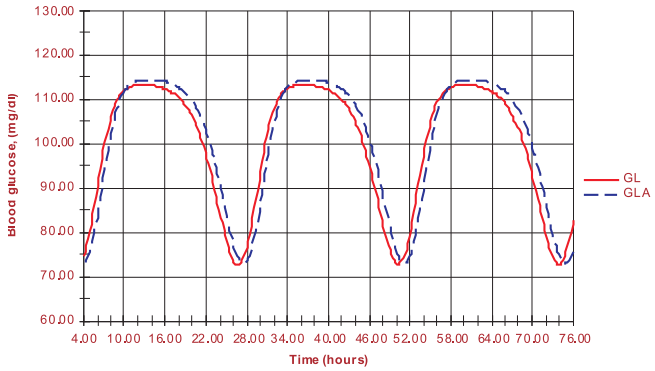

Fig. 6. Comparison of glucoses numerical solution and solution received according to formula (35) in normal cases.

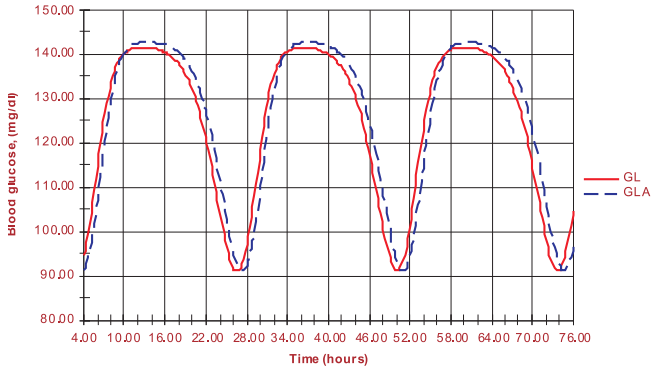

Fig. 7. Comparison of glucoses numerical solution and solution received according to formula (37) in diabetic cases.

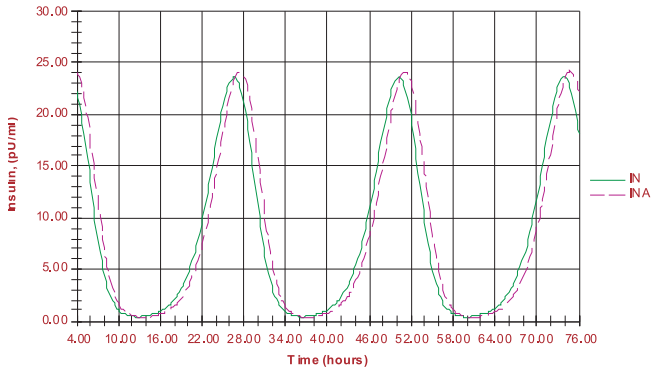

Fig. 8. Comparison of insulin numerical solution and solution received according to formula (34) in normal cases.

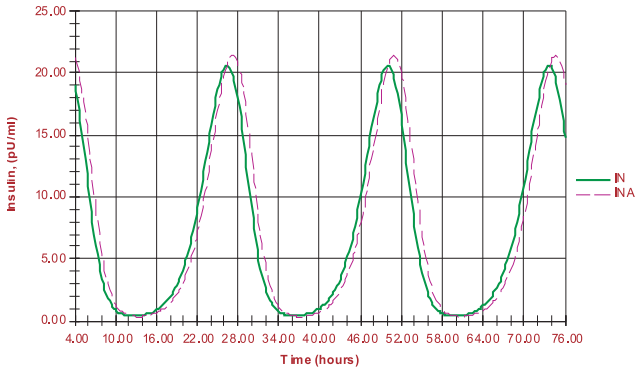

Fig. 9. Comparison of insulin numerical solution and solution received according to formula (36) in diabetic cases.

Further we will introduce diet and physical load functions (1)–(2) into model and on selecting optimal α, γ parameters we will demonstrate graphically variations of glucoses and insulin in normal and diabetes cases, when meals are taken three, four and six times a day and exercises are performed twice a day both in a case of a healthy person and person ill with diabetes.

Values of the parameters h, K_I, K_G, r_G, r_I, c will be taken from the linear analysis. Model (1)–(2) with introduced diet and exercises function is the following:

$$\dot{I}(t) = r_I \left[\frac{G(t)}{K_G} - \frac{I(t-h)}{K_I} \right] I(t), \tag{38}$$

$$\dot{G}(t) = r_G \left[1 + g(t) - f(t) + c \left[1 - \frac{I(t)}{K_I} \right] - \frac{G(t)}{K_G} \right] G(t). \tag{39}$$

Equations (38)–(39) explain the dynamics of physiological system “insulin-sugar” in normal and diabetes cases and allow to describe the dependence of glucose fluctuations from insulin amount. In the model (38)–(39) $i(t)$ and $f(t)$ are takes from Švitra [19]:

$$g(t) = g(t+24) = \sum_{i=1}^{k} g_i(t), f(t) = f(t+24) = \sum_{j=1}^{n} f_j(t), \tag{40}$$

$$g_i(t) = g_i(t+24) = \alpha_i \sin \left[\frac{\pi}{T_i}(t - t_{i1}) \right], \quad t_{i1} \le t \le t_{i2}, \tag{41}$$

$$f_j(t) = f_j(t+24) = \gamma_j \sin \left[\frac{\pi}{T_j}(t - t_{j1}) \right], \quad t_{j1} \le t \le t_{j2}, \tag{42}$$

k – the number of meals, o n – the number of exercises. t_{i1}, t_{j1} – the beginning of the effect. t_{i2}, t_{j2} – the end of the effect. T_i, T_j – duration of the effect, α_i, γ_j – parameters.

On introducing diet and physical exercise functions (1)–(2) into model we modelled numerically the impact of these functions to glucoses and physical exercise variations applying scheme showed in Fig. 1 in normal and diabetes cases. For this purpose we applied the simulation modeling program “Model Maker” (see Figs. 10– 21).

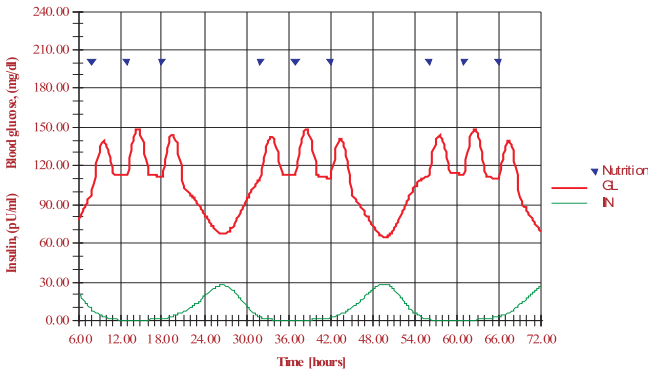

Fig. 10. The glycemic and insulin dynamics of a healthy person taking meal 3 times a day.

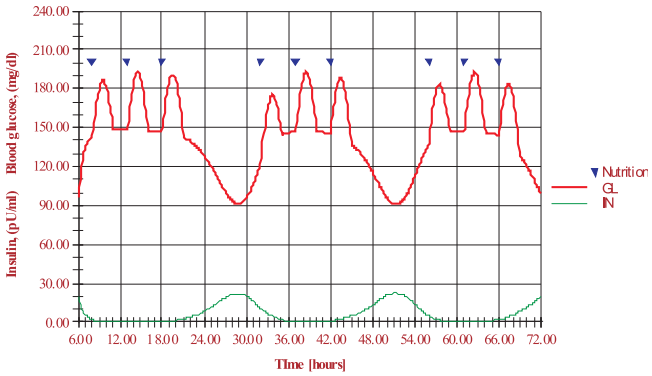

Fig. 11. The glycemic and insulin dynamics of a diabetic taking meal 3 times a day.

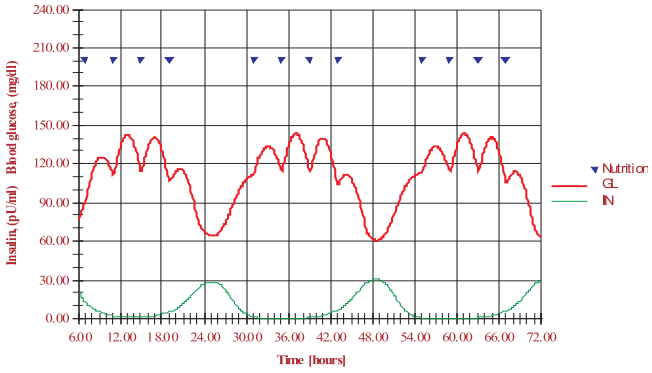

Fig. 12. The glycemic and insulin variation of a healthy person taking meal 4 times a day.

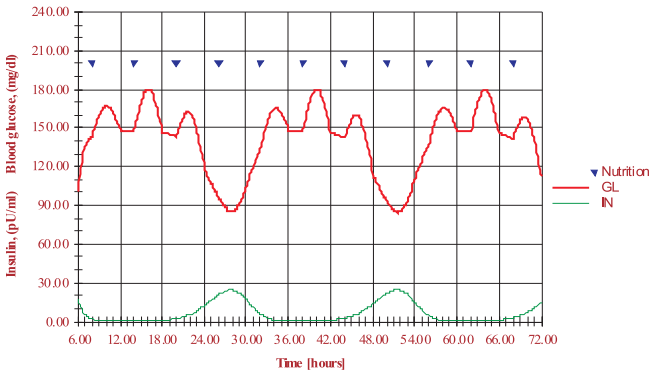

Fig. 13. The glycemic and insulin variation of a diabetic taking meal 4 times a day.

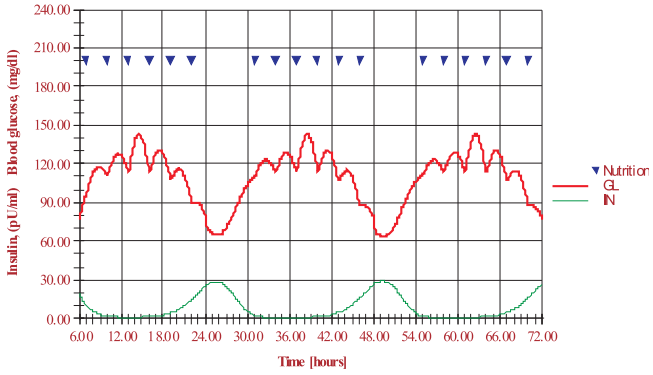

Fig. 14. The glycemic and insulin fluctuations of a healthy person taking meal 6 times a day.

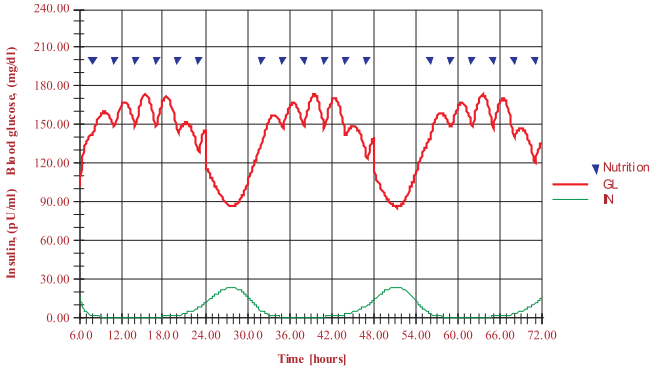

Fig. 15. The glycemic and insulin fluctuations of a diabetic taking meal 6 times a day.

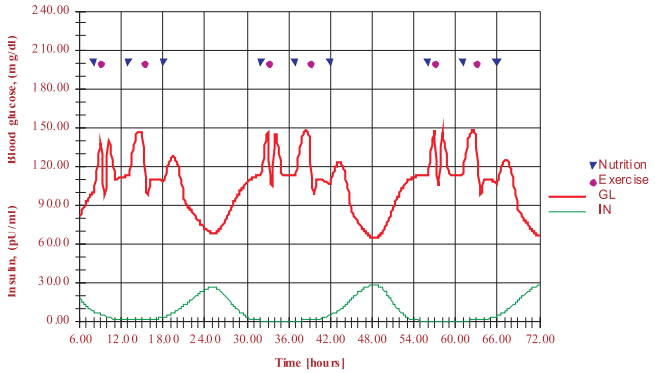

Fig. 16. A healthy person taking meals 3 times a day and exercising 2 times a day.

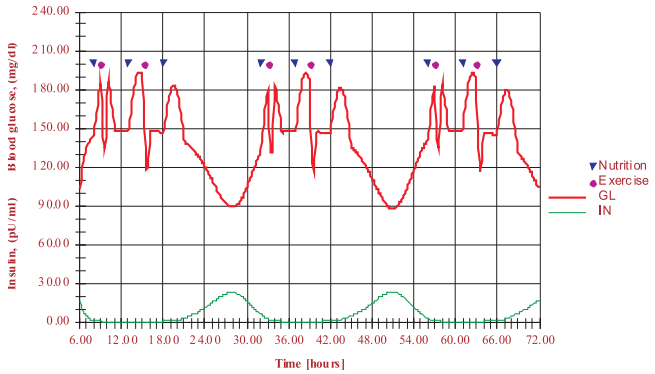

Fig. 17. A diabetic taking meals 3 times a day and exercising 2 times a day.

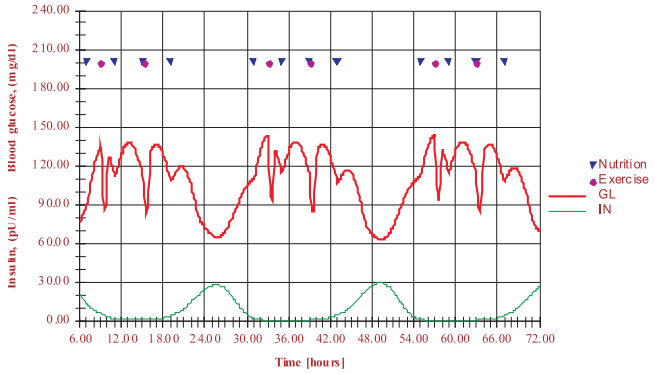

Fig. 18. Glycemic and insulin dynamics of a healthy person taking meals 4 times a day and exercising 2 times a day.

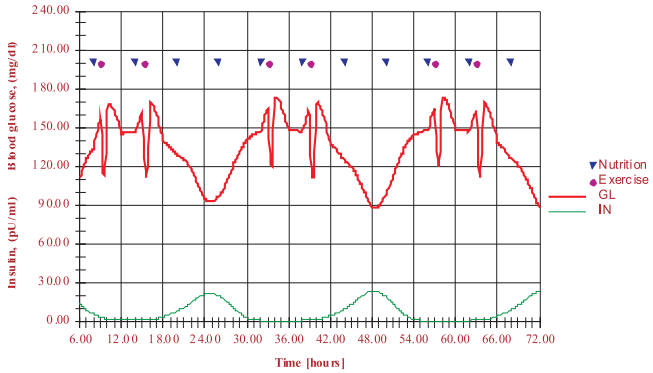

Fig. 19. Glycemic and insulin dynamics of a diabetic taking meals 4 times a day and exercising 2 times a day.

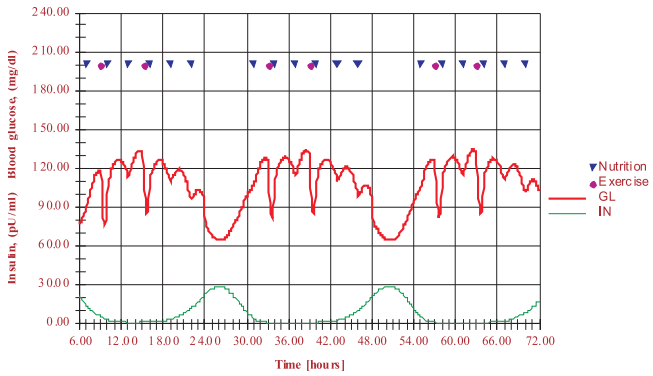

Fig. 20. Numerical solutions (38)–(39) of model when a healthy person takes meals 6 times day and exercises 2 times a day.

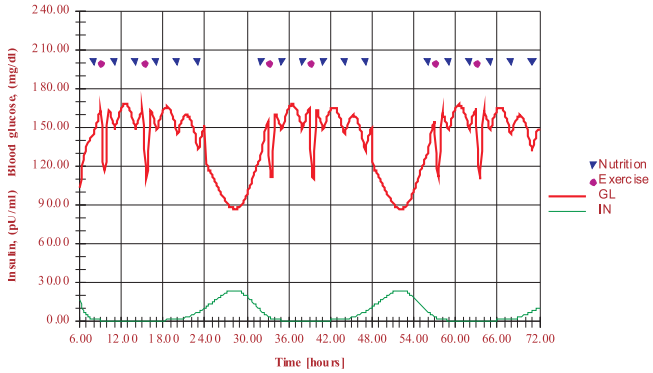

Fig. 21. Numerical solutions (38)–(39) of model when a diabetic takes meals 6 times day and exercises 2 times a day.

Fig. 10 demonstrate the glucose and insulin fluctuations observed in three-day period in normal case when one external force – the diet regime makes impact $k = 3$, $T_i = 3$. In the case of healthy person diet parameters are defined (43).

$$\begin{aligned} &t_{11} = 8, \quad t_{12} = 11, \quad \alpha_1 = 0.30 \quad \text{(breakfast)},\\ &t_{21} = 13, \quad t_{22} = 16, \quad \alpha_2 = 0.35 \quad \text{(dinner)},\\ &t_{31} = 18, \quad t_{32} = 21, \quad \alpha_3 = 0.35 \quad \text{(supper)}. \end{aligned} \tag{43}$$

Fig. 11 shows the glucose and insulin fluctuations observed in three-day period in diabetes case when one external force. i.e. the diet regime makes impact $k = 3$, $T_i = 3$. In case of diabetes the diet parameters are defined (44).

$$\begin{aligned} &t_{11} = 8, \quad t_{12} = 11, \quad \alpha_1 = 0.30 \quad \text{(breakfast)},\\ &t_{21} = 13, \quad t_{22} = 16, \quad \alpha_2 = 0.35 \quad \text{(dinner)},\\ &t_{31} = 18, \quad t_{32} = 21, \quad \alpha_3 = 0.35 \quad \text{(supper)}. \end{aligned} \tag{44}$$

Fig. 12 shows glucose and insulin fluctuations observed in the three-day period in normal case when one external force, i.e the diet regime makes impact $k = 4$, $T_i = 4$. In case of healthy person the diet parameters are defined (45).

$$\begin{aligned} &t_{11} = 7, \quad t_{12} = 11, \quad \alpha_1 = 0.20 \quad \text{(breakfast)},\\ &t_{21} = 11, \quad t_{22} = 15, \quad \alpha_2 = 0.30 \quad \text{(dinner)},\\ &t_{31} = 15, \quad t_{32} = 19, \quad \alpha_3 = 0.30 \quad \text{(afternoon)},\\ &t_{41} = 19, \quad t_{42} = 23, \quad \alpha_4 = 0.20 \quad \text{(supper)}. \end{aligned} \tag{45}$$

Fig. 13 demonstrate glucose and insulin fluctuations observed in three-day period in diabetes case when one external force – the diet regime makes impact $k = 4$, $T_i = 4$. In case of diabetes the diet parameters are defined (46).

$$\begin{aligned} &t_{11} = 8, \quad t_{12} = 12, \quad \alpha_1 = 0.15 \quad \text{(breakfast)},\\ &t_{21} = 14, \quad t_{22} = 18, \quad \alpha_2 = 0.25 \quad \text{(dinner)},\\ &t_{31} = 20, \quad t_{32} = 24, \quad \alpha_3 = 0.20 \quad \text{(supper)},\\ &t_{41} = 26, \quad t_{42} = 30, \quad \alpha_4 = 0.40 \quad \text{(night's lunch)}. \end{aligned} \tag{46}$$

Fig. 14 shows glucose and insulin fluctuations observed in three-day period in normal case when one external force – the diet regime makes impact. $k = 6$, $T_i = 3$. In case of healthy person the diet parameters are defined (47).

$$\begin{aligned} &t_{11} = 7, \quad t_{12} = 10, \quad \alpha_1 = 0.10 \quad \text{(breakfast)},\\ &t_{21} = 10, \quad t_{22} = 13, \quad \alpha_2 = 0.15 \quad \text{(lunch)},\\ &t_{31} = 13, \quad t_{32} = 16, \quad \alpha_3 = 0.30 \quad \text{(dinner)},\\ &t_{41} = 16, \quad t_{42} = 19, \quad \alpha_4 = 0.20 \quad \text{(afternoon)},\\ &t_{51} = 19, \quad t_{52} = 22, \quad \alpha_5 = 0.15 \quad \text{(supper)},\\ &t_{61} = 22, \quad t_{62} = 25, \quad \alpha_6 = 0.10 \quad \text{(night's lunch)}. \end{aligned} \tag{47}$$

Fig. 15 shows glucose and insulin fluctuations observed in three-day period in diabetes case when one external force – diet regime makes impact. $k = 6$, $T_i = 3$. In diabetes case the diet parameters are defined (48).

$$\begin{array}{llll} t_{11} = 8, & t_{12} = 11, & \alpha_1 = 0.10 & \text{(breakfast)}, \\ t_{21} = 11, & t_{22} = 14, & \alpha_2 = 0.15 & \text{(lunch)}, \\ t_{31} = 14, & t_{32} = 17, & \alpha_3 = 0.20 & \text{(dinner)}, \\ t_{41} = 17, & t_{42} = 20, & \alpha_4 = 0.20 & \text{(afternoon)}, \\ t_{51} = 20, & t_{52} = 23, & \alpha_5 = 0.10 & \text{(supper)}, \\ t_{61} = 23, & t_{62} = 26, & \alpha_6 = 0.25 & \text{(night's lunch)}. \end{array} \tag{48}$$

Appropriately tailored physical activity helps diabetics to maintain glycaemia close to normal. Diverse algorithms of physical exercise and diet interaction may be applied while describing diverse diabetes treatment strategies.

Fig. 16 shows glucoses and insulin variations that were observed in the period of three days and nights in normal case when two external forces – diet regime and physical load $k = 3$, $T_i = 3$ make impact and $n = 2$, $T_j = 1$. In this case optimised diet and physical load parameters are defined (49).

$$\begin{array}{llll} t_{11} = 8, & t_{12} = 11, & \alpha_1 = 0.35 & \text{(breakfast)}, \\ t_{21} = 13, & t_{22} = 16, & \alpha_2 = 0.35 & \text{(dinner)}, \\ t_{31} = 18, & t_{32} = 21, & \alpha_3 = 0.30 & \text{(supper)}, \\ t_{11} = 9, & t_{12} = 10, & \gamma_1 = 0.55, & \\ t_{21} = 15, & t_{22} = 16, & \gamma_2 = 0.45. & \end{array} \tag{49}$$

Fig. 17 present glucoses and insulin variations that were observed in the period of three days and nights in diabetes case when two external forces – diet regime and physical exercise $k = 3$, $T_i = 3$ make impact and $n = 2$, $T_j = 1$. In this case optimised diet and physical exercise parameters are defined (50).

$$\begin{array}{llll} t_{11} = 8, & t_{12} = 11, & \alpha_1 = 0.35 & \text{(breakfast)}, \\ t_{21} = 13, & t_{22} = 16, & \alpha_2 = 0.40 & \text{(dinner)}, \\ t_{31} = 18, & t_{32} = 21, & \alpha_3 = 0.25 & \text{(supper)}, \\ t_{11} = 9, & t_{12} = 10, & \gamma_1 = 0.50, & \\ t_{21} = 15, & t_{22} = 16, & \gamma_2 = 0.40. & \end{array} \tag{50}$$

Fig. 18 offer glucoses and insulin variations that were observed in the period of three days and nights in normal case when two external forces – diet regime and physical load $k = 4$, $T_i = 4$ make impact and $n = 2$, $T_j = 1$. In this case optimised diet and

physical load parameters are defined (51).

$$\begin{array}{llll} t_{11}=7, & t_{12}=11, & \alpha_1=0.30 & \text{(breakfast)},\\ t_{21}=11, & t_{22}=15, & \alpha_2=0.25 & \text{(dinner)},\\ t_{31}=15, & t_{32}=19, & \alpha_3=0.25 & \text{(afternoon)},\\ t_{41}=19, & t_{42}=23, & \alpha_4=0.20 & \text{(supper)},\\ t_{11}=9, & t_{12}=10, & \gamma_1=0.5, & \\ t_{21}=15, & t_{22}=16, & \gamma_2=0.5. & \end{array} \tag{51}$$

Fig. 19 present glucoses and insulin variations that were observed in the period of three days and nights in diabetes case when two external forces – diet regime and physical exercise $k=3$, $T_i=4$ make impact and $n=2$, $T_j=1$. In this case optimised diet and physical exercise parameters are defined (52).

$$\begin{array}{llll} t_{11}=8, & t_{12}=12, & \alpha_1=0.20 & \text{(breakfast)},\\ t_{21}=14, & t_{22}=18, & \alpha_2=0.20 & \text{(dinner)},\\ t_{31}=20, & t_{32}=24, & \alpha_3=0.10 & \text{(supper)},\\ t_{41}=26, & t_{42}=30, & \alpha_4=0.50 & \text{(night's lunch)},\\ t_{11}=9, & t_{12}=10, & \gamma_1=0.55, & \\ t_{21}=15, & t_{22}=16, & \gamma_2=0.45. & \end{array} \tag{52}$$

Fig. 20 offer glucoses and insulin variations that were observed in the period of three days and nights in normal case when two external forces – diet regime and physical load $k=6$, $T_i=3$ make impact and $n=2$, $T_j=1$. In this case optimised diet and physical load parameters are defined (53).

$$\begin{array}{llll} t_{11}=7, & t_{12}=10, & \alpha_1=0.15 & \text{(breakfast)},\\ t_{21}=10, & t_{22}=13, & \alpha_2=0.15 & \text{(lunch)},\\ t_{31}=13, & t_{32}=16, & \alpha_3=0.20 & \text{(dinner)},\\ t_{41}=16, & t_{42}=19, & \alpha_4=0.15 & \text{(afternoon)},\\ t_{51}=19, & t_{52}=22, & \alpha_5=0.15 & \text{(supper)},\\ t_{61}=22, & t_{62}=25, & \alpha_6=0.20 & \text{(night's lunch)},\\ t_{11}=9, & t_{12}=10, & \gamma_1=0.55, & \\ t_{21}=15, & t_{22}=16, & \gamma_2=0.45. & \end{array} \tag{53}$$

Fig. 21 show glucoses and insulin variations that were observed in the period of three days and nights in diabetes case when two external forces – diet regime and physical exercise $k=6$, $T_i=3$ make impact and $n=2$, $T_j=1$. In this case optimised diet and

physical exercise parameters are defined (54).

$$\begin{array}{llll}
t_{11}=8, & t_{12}=11, & \alpha_1=0.15 & \text{(breakfast)},\\
t_{21}=11, & t_{22}=14, & \alpha_2=0.15 & \text{(lunch)},\\
t_{31}=14, & t_{32}=17, & \alpha_3=0.15 & \text{(dinner)},\\
t_{41}=17, & t_{42}=20, & \alpha_4=0.15 & \text{(afternoon)},\\
t_{51}=20, & t_{52}=23, & \alpha_5=0.15 & \text{(supper)},\\
t_{61}=23, & t_{62}=26, & \alpha_6=0.25 & \text{(night's lunch)},\\
t_{11}=9, & t_{12}=10, & \gamma_1=0.44, & \\
t_{21}=15, & t_{22}=16, & \gamma_2=0.56. &
\end{array} \tag{54}$$

In this section we demonstrated how the model (1)–(2) could be applicable simulated of glycemic and insulin dynamics introduced functions of nutritional and physical exercise in order to work out optimal of diabetes control.

3 Conclusions

A linear and nonlinear analysis of model (1)–(2) was performed following qualitative methods of bifurcation theory. On selecting parameter values implying a certain biological meaning in internal equilibrium state environment the existence of stable periodic solutions obtained applying the simulation modeling program "Model Maker" in a numerical way was demonstrated.

Applying D-decomposition method a stability sphere of asymptotic stability $D_2 = (\pi/12; 5\pi/12)$ where a single one frequency approximate stable periodical solution of model (1)–(2) exists and its analytical notation is constructed, was defined.

A constructed approximate stable periodical solution of the model coincides with numerical solution well enough.

On introducing two external forces specifying diet and physical exercise functions in normal and diabetes cases the received results of numerical analyses showed that this model reflects glycaemia and insulin dynamics of a healthy person and person ill with diabetes rather exactly.

On comparing received numerical solutions of these models with experimental data a fairly good coincidence of the models and the data was received and this fact allows to apply the investigated model in monitoring complex systems.

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