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Research article

MATHEMATICAL MODEL TO DESCRIBE REGULATION OF CARBOHYDRATE METABOLISM TAKING INTO ACCOUNT FUNCTIONAL DISORDERS FOR PREDICTING INCREASED RISK OF ASSOCIATED DISEASES

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Diseases of the endocrine system, including those associated with increased consumption of carbohydrates and high-calorie foods, are common throughout the world. Existing complex mathematical models for describing carbohydrate metabolism processes contain many parameters, which makes their use difficult at the individual level. The aim of this work is to develop a mathematical model to describe regulation of carbohydrate metabolism, taking into account the endocrine function of the pancreas and functional disorders in the body under various diets. The new basic mathematical formulation proposed by the authors of this article takes into account the main processes in the system of glucose, insulin and glucagon balance in blood and glucose in the liver as well as functional disorders of certain organs (liver, kidneys, pancreas), time delays in the transmission of regulatory signals, as well as various diets (fast food with a high content of fast carbohydrates, high-calorie food, and unbalanced daily diets). A system of differential equations with a delayed argument is used as a mathematical apparatus and the Euler method is used for the numerical solution of the system.

Numerical experiments consider the results for four scenarios: a process without functional disorders in the body; impaired pancreatic and liver function in type I diabetes; impaired insulin-dependent glucose intake in type II diabetes; and unbalanced consumption of fast carbohydrates. In case of diabetes or when consuming fast carbohydrates, periods of elevated blood glucose as well as excess levels themselves (up to 8.8–15 mmol/l) are significantly higher than in case the disease is absent. Elevated glucose levels and periods of exceeding normal levels are the output parameters of the model, risk-inducing factors of diseases of the endocrine and cardiovascular systems. In addition, the carbohydrate balance is violated in scenarios with diabetes. The body begins to store excess glucose in the liver on a daily basis, which can lead to further conversion of carbohydrates into fats, increasing the obesity risk.

Depending on the simulation results, disease prevention measures can include optimal individual recommendations for balancing the amount of consumed carbohydrates and meals per day. In future studies, it is advisable to consider carbohydrate metabolism in combination with fat, which allows for more detailed consideration of pathways typical for diabetes and concomitant pathologies.

Keywords: *mathematical model, carbohydrate metabolism, diabetes mellitus, insulin, glucose, glucagon, liver, functional disorders, fast carbohydrates, unbalanced diet, risk.*

Endocrine, nutritional and metabolic diseases are the most influenced by external exposures. Multiple studies, both Russian and foreign ones, consider a diet a major factor of hyperglycemia, overweight, obesity, and, consequently, type 2 diabetes mellitus [1, 2]. As reported in research literature, diets with high levels of fats, carbohydrates and high total caloric contents are the primary risk factor of the disease. Most experts believe changes in eating behaviors to be a trustworthy strategy aimed at reducing likelihood of endocrine diseases [3]. Diseases involving high blood sugar levels belong to metabolic disorders[1]. The WHO (World Health Organization) reported (2022) more than 800 million people diag-

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[1] Potemkin V.V. Endokrinologiya [Endocrinology]. Moscow, Meditsina Publ., 1986, 432 p. (in Russian).

nosed with diabetes across the globe, which is approximately 10 % of the global population. Diabetes mellitus is a group of metabolic diseases involving hyperglycemia, which is caused by defective insulin secretion, weakened insulin effects or both these factors [4].

Type 1 diabetes mellitus is associated with defective insulin secretion due to destruction of insulin-producing ß-cells. It is more often diagnosed in young patients aged below 30 years and involves damage to more than 80 % of insulin-making cells[2]. Diabetes pathways include autoimmune pancreas damage after a virus infection or exposure to toxicants. In type 2 diabetes mellitus, tissues are insensitive to insulin effects and blood insulin can be normal or elevated. Most patients (85 %) are diagnosed with type 2 diabetes mellitus. Obesity makes tissues less sensitive to insulin since fat tissues create an additional blockade of insulin effects [5].

Two pancreas hormones, insulin and glucagon, are two major components responsible for regulating blood sugar levels. Growing glucose levels in blood stimulate insulin release. The pancreas releases glucagon when blood sugar falls too low. Glucagon increases blood glucose by enhancing glycogen transport from the liver and insulin promotes more intensive glucose use by various tissues [6].

Mathematical models are developed to describe interaction between insulin and glucose; they allow operative predictive descriptions of processes under various scenarios. A model presented by R. Hovorka with colleagues [7] describes the kinetics of glucose upon intravenous administration allowing for its distribution between plasma and tissues, insulin independent and insulin dependent consumption, as well as suppressed glucose production by the liver due to insulin effects. Overall, the model consists of 9 ordinary differential equations and 15 parameters. The model parameters were either obtained by clinical studies involving patients with type 1 diabetes mellitus or taken from distributions of likelihoods in a population. A model suggested by J.T. Sorensen[3] also uses a chamber approach. This model was initially developed to describe processes in a healthy body using 22 non-linear differential equations including 3 equations to describe endogenous insulin secretion. The parameter values were derived from literature and taken for an average person.

A model developed by P.G. Fabietti with colleagues [8] allows for glucose introduction in blood from the gastrointestinal tract (GIT) considering both fast carbohydrates (fast or simple carbs) and slow ones (slow or complex carbs). The model peculiarity is sinusoidal representation of circadian variability of insulin sensitivity. Four out of 14 model parameters were estimated based on clinical data. This model is a modification of the so called ‘minimal model’ [9], one of the simplest ones for more or less adequate description of insulin – glucose interaction upon intravenous glucose administration.

A model presented in a work by M. Lombarte et al. [10] was developed to describe glucose and insulin homeostasis in healthy rats using a system of equations, which covered glucose introduction from the GIT, glucose use by tissues, glucose production by the liver, insulin secretion, insulin clearance, and a balance between basal glucose and insulin levels. The model has several limitations including its applicability only to healthy rats, an oversimplified concept of glucose regulation without allowing for effects produced by other hormones or individual variations, absence of retardation times and inability to simulate insulin resistance, which is a key pathway in type 2 diabetes mellitus. The model is useful for examining basic pathways of glucose homeostasis but its predictive value is limited due to failure to consider complex regulatory interactions and pathological states. Moreover, an issue of transferring the simulation results onto the human body seems complicated.

[2] Balabolkin M.I. Diabetologiya [Diabetology]: manual. Moscow, Meditsina Publ., 2000, 672 p. (in Russian).

[3] Sorensen J.T. A physiologic model of glucose metabolism in man and its use to design and assess improved insulin therapies for diabetes: Ph.D. dissertation. Massachusetts, Massachusetts Institute of Technology, 1985, 556 p.

A model described by C. Dalla Man and others [11] provides a detailed description of glucose regulation but includes too many mathematical equations (12 nonlinear differential equations and 18 algebraic equations) and requires complex methods for estimating multiple parameters. It is noteworthy that the fastest feedback loop consists in a release of stored insulin immediately after glucose stimulus via elevated blood glucose concentrations[4]. This first insulin peak reaches its maximum after about three to five minutes after glucose administration. The second feedback loop is due to the glucose dependent enhancement of insulin provision. This has a visible effect after about 10 minutes[4]. In this respect, it is important to allow for retardation times when developing mathematical models.

A model developed by M. Gallenberger with colleagues [12] allows for a constant growth in the glucose introduction rate in blood due to the difference between introduction from the liver and consumption by the brain and nerve tissues. The decline rate for blood glucose is described by summands, which cover both insulin independent and insulin dependent consumption by other organs. Blood insulin dynamics is described through the difference between secretion and excretion rates. Some models that describe the regulatory glucose – insulin system are presented, for example, in works [13, 14]. They describe not only glucose and insulin mass dynamics but also allow for changes in β-cell counts.

A model suggested by N.A. Shirokova [15, 16] describes the insulin – glucose balance in diabetes mellitus by using a system of two differential equations and allowing for glucose intake with food, critical levels to describe glucose excretion by the kidneys in hyperglycemia, insulin dependent glucose consumption, and glucose production by the liver. It is worth noting that the model developed by N.A. Shirokova, just as some other models, does not consider insulin independent glucose consumption.

To sum up the review results, we deem it advisable to divide the models into basic ones, which consider only basic system elements, and complex ones, which cover intermediate stages of element transformation and additional processes.

Tables 1 and 2 provide the results obtained by comparing existing basic models that describe hormonal blood sugar regulation as well as types of basic summands used in a mathematical model suggested by the authors of a given work. More complex models[5] [7, 10, 11] share some disadvantages, primarily, too many parameters and the necessity to accomplish multiple additional metabolic studies for their estimation. This creates the necessity to use mean values in numeric computations thereby decreasing authenticity of modeling results and limiting model applicability at the individual level.

If we analyze Tables 1 and 2, we can see that glucose introduction in blood is either believed to be a constant or is described by a certain function of time reflecting food consumption and glucose absorption from the GIT into blood. Glucose release in blood, insulin independent consumption as well as glucose production by the liver are described in fewer studies, which means that these processes are often neglected. Insulin dynamics is described in many basic models by using similar summands. A new basic model suggested by us covers all the foregoing processes as well as additional regulatory effects produced by glucagon by adding relevant summands into our equations and the mathematical statement. In addition, we have introduced some organ dysfunctions (liver, kidneys, and pancreas) and time retardations in transfer of regulatory signals into our model. It also allows for various diets (fast food with high levels of simple carbs, food with high caloric contents and imbalanced daily diets).

[4] Grodsky G.M. A threshold distribution hypothesis for packet storage of insulin and its mathematical modeling. *J. Clin. Invest.*, 1972, vol. 51, no. 8, pp. 2047–2059. DOI: 10.1172/JCI107011

[5] Sorensen J.T. A physiologic model of glucose metabolism in man and its use to design and assess improved insulin therapies for diabetes: Ph.D. dissertation. Massachusetts, Massachusetts Institute of Technology, 1985, 556 p.

Table 1

Comparison of basic mathematical models (summands for glucose in equations)

Reference	Glucose consumption	Glucose intake	Glucose excretion	Glucose production by the liver
K. Millsaps et al. [6]	$-K_6 C_{gl}^{bl} C_{ins}^{bl}$	–	–	–
A. De Gaetano et al. [14]	$-K_1 C_{gl}^{bl} - K_6 C_{gl}^{bl} C_{ins}^{bl}$	$K = const$	–	–
N.A. Shirokova [15]	$-K_6 C_{gl}^{bl} C_{ins}^{bl}$	$f(t)$	$-K_1 \left\langle \left(C_{gl}^{bl} - C_{gl}^{bl**} \right) \right\rangle$	$K_4 < (C_{gl}^{bl*} - C_{gl}^{bl}) >$
J. Hussain et al. [17]	$-K_1 C_{gl}^{bl} - K_6 C_{gl}^{bl} C_{ins}^{bl}$	$K = const$	–	–
M. Lombarte et al. [10]	$-K_{10} - K_6 C_{ins}^{bl}$	$f(t)$	–	$K_4 < (C_{gl}^{bl*} - C_{gl}^{bl}) >$
M. Gallenberger et al. [12]	$-K_1 C_{gl}^{bl} - K_6 C_{gl}^{bl} C_{ins}^{bl}$	$f(t)$	–	–
This article	$-K_{10} - \frac{K_6 C_{gl}^{bl}(t) C_{ins}^{bl}(t)}{K_7 + C_{gl}^{bl}(t)}$	$f(t)$	$-K_1 F_k C_{gl}^{bl}(t)$	$-\left\langle \left(C_{gl}^{bl}(t-t_1) - C_{gl}^{bl*} \right) \right\rangle K_4 F_{liv}$ $+C_{gn}^{bl}(t-t_2) \cdot$ $\cdot \left\langle \left(C_{gl}^{bl**} - C_{gl}^{bl}(t-t_3) \right) \right\rangle K_5 F_{liv}$

Note: *denominations are explained in the section Conceptual and Mathematical Statement.

Table 2

Comparison of basic mathematical models (summands for insulin in equations)

Reference	Insulin production	Insulin secretion
K. Millsaps et al.[6]	$K_2 C_{gl}^{bl}$	$-K_3 C_{ins}^{bl\,2}$
A. De Gaetano et al. [14], J. Hussain et al. [17], M. Lombarte et al. [10], M. Gallenberger et al. [12]	$K_2 C_{gl}^{bl}$	$-K_3 C_{ins}^{bl}$
N.A. Shirokova [15]	$K_2 \left\langle (C_{gl}^{bl} - C_{gl}^{bl*}) \right\rangle$	$-K_3 C_{ins}^{bl} C_{gl}^{bl}$
This article	$K_2 F_{pn1} C_{gl}^{bl}(t-t_4) C_{gn}^{bl}(t-t_5)$	$-K_3 F_k C_{ins}^{bl}(t)$

Note: *denominations are explained in the section Conceptual and Mathematical Statement.

The aim of this work is to develop a mathematical model to describe regulation of carbohydrate metabolism, taking into account the endocrine function of the pancreas and functional disorders in the body under various diets.

The work contains an informative statement together with describing the analyzed physiological process; a new conceptual statement with creating a structural scheme of the process; a mathematical statement that includes equations to describe the glucose, insulin and glucagon balance in blood and glucose in the liver; approaches to identifying model parameters; a numeric solution and analysis of the results with their verification.

The study is accomplished as a part of developing the comprehensive multi-level model of accumulating functional disorders in the human body developed by the team of authors [18]. The meso-level of the model considers physiological and pathological processes in specific organs and systems including the respiratory, digestive [19], cardiovascular and

[6] Millsaps K., Pohlhausen K. A mathematical model for glucose-insulin interaction. *Mathematical Biosciences*, 1975, vol. 23, no. 3–4, pp. 237–251. DOI: 10.1016/0025-5564(75)90038-3

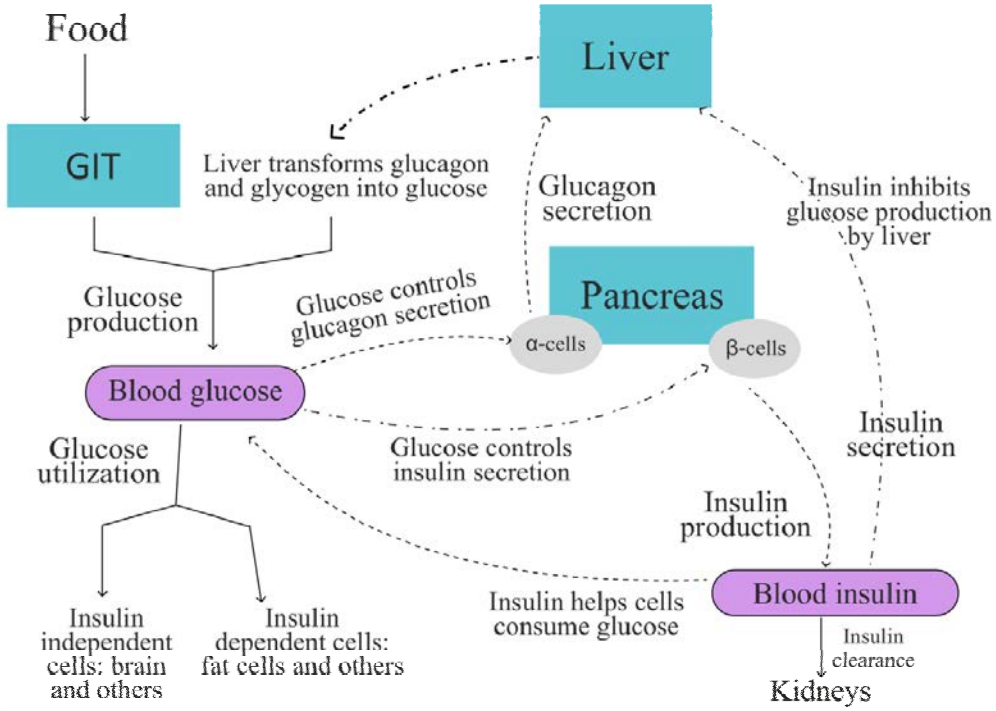

Figure 1. A scheme of carbohydrate metabolism regulation

neuroendocrine ones. Numeric computations accomplished by using the developed model of the stomach and duodenum at the meso-level allow detecting zones with elevated acidity with high reliability; such zones are a known risk factor of developing dystrophic changes in mucosa [20]. A model that describes carbohydrate metabolism is suggested in the present work; it is associated with the digestion model through glucose flow from the GIT into blood. High blood sugar and periods of it being above the safe level are output model parameters and risk-inducing factors for endocrine and cardiovascular diseases.

Conceptual and mathematical statement. Figure 1 provides a scheme of carbohydrate metabolism regulation considering the basic system elements.

The following conceptual hypotheses were employed when building the model:

- Mathematical statement involves using retarded differential equations (RDE);
- Intensity of insulin production by the pancreas is proportionate to blood glucose and glucagon;
- Glucose is uninterruptedly consumed in the body by tissues and organs; intensity of glucose utilization is described by two components. The first one is proportionate to insulin and glucose levels allowing for saturation (insulin dependent consumption); the second one is proportionate to a glucose concentration (insulin independent consumption);
- When blood glucose falls below its normal level, it is released from the liver by effects produced by glucagon to maintain its proper level in blood; when blood sugar is high, the inverse process occurs;
- Glucose, glucagon and insulin are excreted from the body by the kidneys and their excretion rate is proportionate to their relevant concentrations;
- Glucagon secretion rate is inversely proportionate to insulin and glucose levels, which ensures the feedback within the regulatory loop.

The following variables are used in this study to investigate carbohydrate metabolism: blood glucose (C_{gl}^{bl}), blood insulin (C_{ins}^{bl}), blood glucagon (C_{gn}^{bl}), as well as a glucose level in the liver (C_{gl}^{liv}), which is stored in the organ as glycogen.

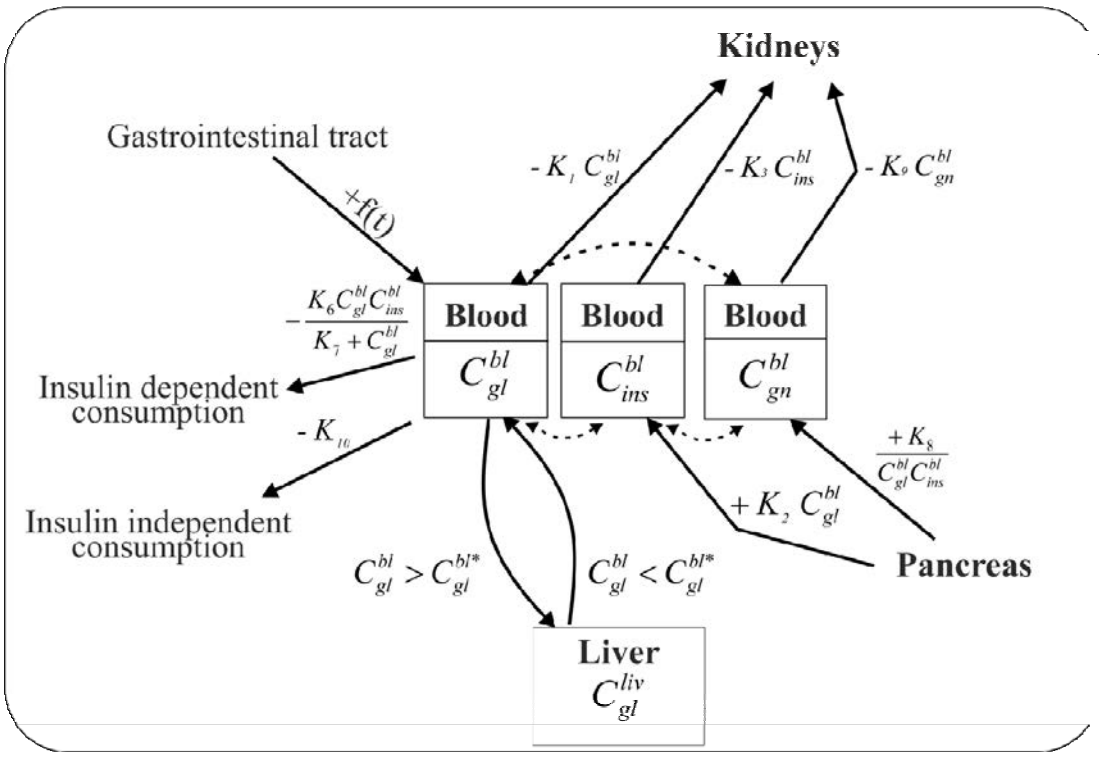

Figure 2. Conceptual scheme to describe carbohydrate metabolism

Considering these denominations and foregoing hypotheses, we have developed a conceptual scheme to describe carbohydrate metabolism given in Figure 2.

A system of RDE (retarded differential equations) is used in the mathematical statement to describe dynamics of four foregoing variables written as follows:

$$\frac{dC_{gl}^{bl}}{dt} = f(t) - K_1 F_k C_{gl}^{bl}(t) - \left(C_{gl}^{bl}(t-t_1) - C_{gl}^{bl*}\right) K_4 F_{liv} + C_{gn}^{bl}(t-t_2)\left(C_{gl}^{bl**} - C_{gl}^{bl}(t-t_3)\right) K_5 F_{liv} - \frac{K_6 C_{gl}^{bl}(t) C_{ins}^{bl}(t)}{K_7 + C_{gl}^{bl}(t)} - K_{10}, \quad (1)$$

$$\frac{dC_{ins}^{bl}}{dt} = K_2 F_{pn1} C_{gl}^{bl}(t-t_4) C_{gn}^{bl}(t-t_5) - K_3 F_k C_{ins}^{bl}(t), \quad (2)$$

$$\frac{dC_{gn}^{bl}}{dt} = \frac{K_8 F_{pn2}}{C_{gl}^{bl}(t-t_6) C_{ins}^{bl}(t-t_7)} - K_9 F_k C_{gn}^{bl}(t), \quad (3)$$

$$\frac{dC_{gl}^{liv}}{dt} = \left\langle \left(C_{gl}^{bl}(t-t_1) - C_{gl}^{bl*}\right) \right\rangle K_4 F_{liv} - C_{gn}^{bl}(t-t_2) \left\langle \left(C_{gl}^{bl**} - C_{gl}^{bl}(t-t_3)\right) \right\rangle K_5 F_{liv}, \quad (4)$$

where K_1 is the coefficient that describes the glucose excretion rate by the kidneys, 1/s;

K_2 is the coefficient that reflects insulin secretion rate by the pancreas, L · μU /(s · mmol^2);

K_3 is the coefficient that describes insulin excretion rate by the kidneys, 1/s;

K_4 and K_5 are the coefficients that describe rates of glucose flow between blood and the liver, 1/s, L/(s · mmol); in case blood glucose C_{gl}^{bl} is higher than the critical value C_{gl}^{bl*}, the glucose flows from blood into the liver; in case blood glucose C_{gl}^{bl} is below the critical value C_{gl}^{bl**}, then glucose flows from the liver into blood;

K_6 and K_7 are the coefficients that reflect the rate of insulin dependent glucose consumption by the body (nutrition), mmol/(s · μU), mmol/L;

f(t) is the function of glucose introduction into blood from the gastrointestinal tract depending on time;

K_8 is the coefficient that describes the glucagon secretion rate by the pancreas ($mmol^2 \cdot \mu U)/(s \cdot L^3$);

K_9 is the coefficient that describes the glucagon excretion rate by the kidneys, 1/s;

K_{10} is the coefficient that reflects the rate of insulin independent glucose consumption by the body, mmol/(s · L);

F_k is the kidney function quality;

F_{liv} is the liver function quality;

F_{pn1} is the pancreas function quality in insulin production;

F_{pn2} is the pancreas function quality in glucagon production;

t_i is the retardation coefficient, i values vary between 1 and 7;

$< >$ are Macaulay brackets; if the argument is negative, the whole expression evaluates to zero and if the argument is positive it is used as is.

The left parts in the equations are derivatives from the variables per time (rates of changes in concentrations). The fourth equation contains summands that describe the rates of glucose metabolism between blood and the liver similar per their modules to those given in the first equation but with the inverse sign. Any organ dysfunctions will lead to adjustments in rates of changes in the variables in those summands where function quality acts as an additional multiplier with its value ranging between 0 and 1. When the liver function quality declines, glucose deposition rates and rates of release from the liver depot also go down; when the kidney function quality decreases, excretion rates also decline for the substances; when the pancreas function quality deteriorates, hormone (insulin and/or glucagon) production declines as well. In addition, the model can allow for GIT dysfunctions by changing the function that describes carbohydrate intake in blood $f(t)$. Moreover, by regulating the shape of the function $f(t)$, we can describe various unhealthy diets and irregular meal times, allow for introduction of slow and fast carbs in blood including cases when it is imbalanced over time.

The results of numeric experiments and their discussion. In this study, four scenarios are considered; they describe various states of the body and diets. The first three scenarios consider a balanced daily diet with predominant consumption of slow carbs relative to fast ones. The fourth scenario describes an imbalanced diet with fast carbs prevailing in it relative to slow ones.

1. The first (baseline) scenario describes the process without any functional disorders in the body and the function quality is taken as equal to 1 for all the organs.

2. The second scenario describes a situation with type 1 diabetes mellitus. In this disease, the pancreas is unable to produce insulin in sufficient amounts. In this scenario, the pancreas function quality is decreased and is equal to $F_{pn1} = 0.5$, which corresponds to a considerable decline in insulin production leading to diabetes mellitus. In addition, $F_{liv} = 0.5$, which corresponds to the relevant decline in the liver function associated with transforming glucose into glycogen and vice versa.

3. Type 2 diabetes mellitus is considered in the third scenario. In this case, the body becomes less sensitive to insulin effects, which also leads to high blood sugar. However, in contrast to type 1 diabetes mellitus, the pancreas continues to produce insulin. In the third scenario, the coefficient K_6 is reduced by six times; this means, that glucose utilization by insulin is impaired by 83 %.

4. The fourth scenario considers the process without any dysfunctions but the function for carbohydrate introduction into blood $f(t)$ differs from the first three scenarios and describes consumption of fast carbs.

After the parameters have been identified in the first approximation, the plan is to use some averaged coefficients that describe normal carbohydrate metabolism. At this stage in the study, the models are selected in such a way so that insulin and glucose levels are within their physiological ranges in the baseline scenario when any dysfunctions are absent in the body and a consumed diet is well balanced. Table 3 provides the model parameters for all four scenarios. In the first approximation, the $f(t)$ is considered a function describing how glucose enters blood from the gastrointestinal tract depending on time and is determined by a piecewise set function:

Table 3

Model parameters: values

Parameter	Values	Measuring units	Parameter	Values (scenario 1–3; scenario 4)	Measuring units
Individual coefficients			Parameters of glucose introduction function		
K_1	1.00E-05	1/s	$f_{1\max}$	1.10E-02; 2.20E-02	mmol/(s·L)
K_2	2.00E-03	L · μU / (s · mmol^2)	$f_{2\max}$	1.30E-02; 4E-02	mmol^2/(s·L)
			$f_{3\max}$	1.20E-02; 3.7E-02	mmol/(s·L)
K_3	5.00E-03	1/s	a_0	1.02E-03; 2.8E-07	mmol /(s^2·L)
			b_0	-6.16E-01; -2.36	mmol/(s·L)
K_4	3.0E-03	1/s	a_1	1.02E-03; 2.2E-02	mmol /(s^2·L)
K_5	1.00E-03	L/(s · mmol)	b_1	-6.16E-01; -1.76E-01	mmol/(s·L)
K_6	3.00E-04	mmol/(s · μU)	a_2	5.50E-03; 3.37E+05	mmol /(s^2·L)
K_7	4	mmol/L	b_2	-4.40E-02; -1.84	mmol/(s·L)
K_8	9.00E-03	(mmol^2· мкЕд)/(s · L^3)	a_3	3.37; 4E-02	mmol /(s^2·L)
K_9	1.00E-04	1/s	b_3	-5.73E-01; -5.2E-01	mmol/(s·L)
			a_4	5.51E-03; 2.59E+13	mmol /(s^2·L)
			b_4	-6.97E-02; -2.44	mmol/(s·L)
K_{10}	2.70E-03	mmol/(s·L)	a_5	2.44E+02; 3.7E-02	mmol /(s^2·L)
			b_5	-6.56E-01; -6.66E-01	mmol/(s·L)
			a_6	5.09E-03; 1E+18	mmol /(s^2·L)
			b_6	-8.98E-02; -2.36	mmol/(s·L)

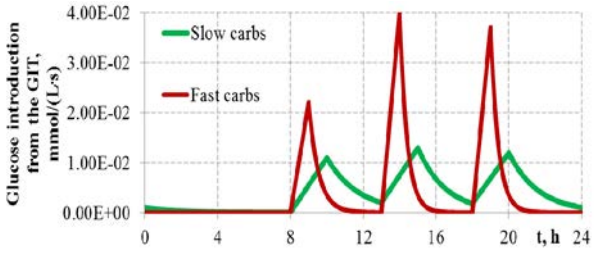

Figure 3. Graph of the function that describes glucose introduction in blood from the GIT *f(t)*

a linear equation when the flow is growing ($f(t) = at + b$) and an exponential equation when the flow is declining ($f(t) = ae^{bt}$). Figure 3 provides the graph of the function that corresponds to three meals. The parameters $f_{i\max}$ in Table 1 correspond to the maximum values of the function *f(t)* after the *i*-th meal.

In the first three scenarios, the maximum values $f_{i\max}$ are close for all meals, which describes more even introduction of carbohydrates in blood; the function reaches its peak values 2 hours after a meal and the function of carbohydrate introduction approaches 0 after another 2 hours. This pattern is typical when slow carbs are consumed. In the fourth scenario, carbohydrate introduction in blood is less balanced during meals since the smallest amount is consumed during the first meal (breakfast) whereas it grows considerably during the second and third meals (lunch and dinner); peak values are usually reached one hour after a meal and the carbohydrate flow into blood is depleted significantly after another hour. Shorter peaks with greater amplitude are typical when simple carbs are consumed. With the preset parameters, the total carbohydrate flow from the GIT into blood amounts to approximately 305 g over 24 hours for all scenarios, which is consistent with average consumption norms.

At this stage, the same initial conditions are set in the model for each of the first three scenarios: $C_{gl}^{bl}(t = 0) = 4.5$ mmol/L; $C_{ins}^{bl}(t = 0) = 2.6$ μU/mL; $C_{gl}^{liv}(t = 0) = 400$ mmol/L; $C_{gn}^{bl}(t = 0) = 3$ mmol/L. The retardation times t_1, t_2, t_3 are taken as equal to 60 s, t_4, $t_5 = 180$ s, t_6, $t_7 = 240$ s.

Numeric solution to the equations relies on using the Euler method with a time step equal to 4 s. The results are obtained for the time period between 0 and 24 hours. The computation results for all four scenarios are given in Figure 4.

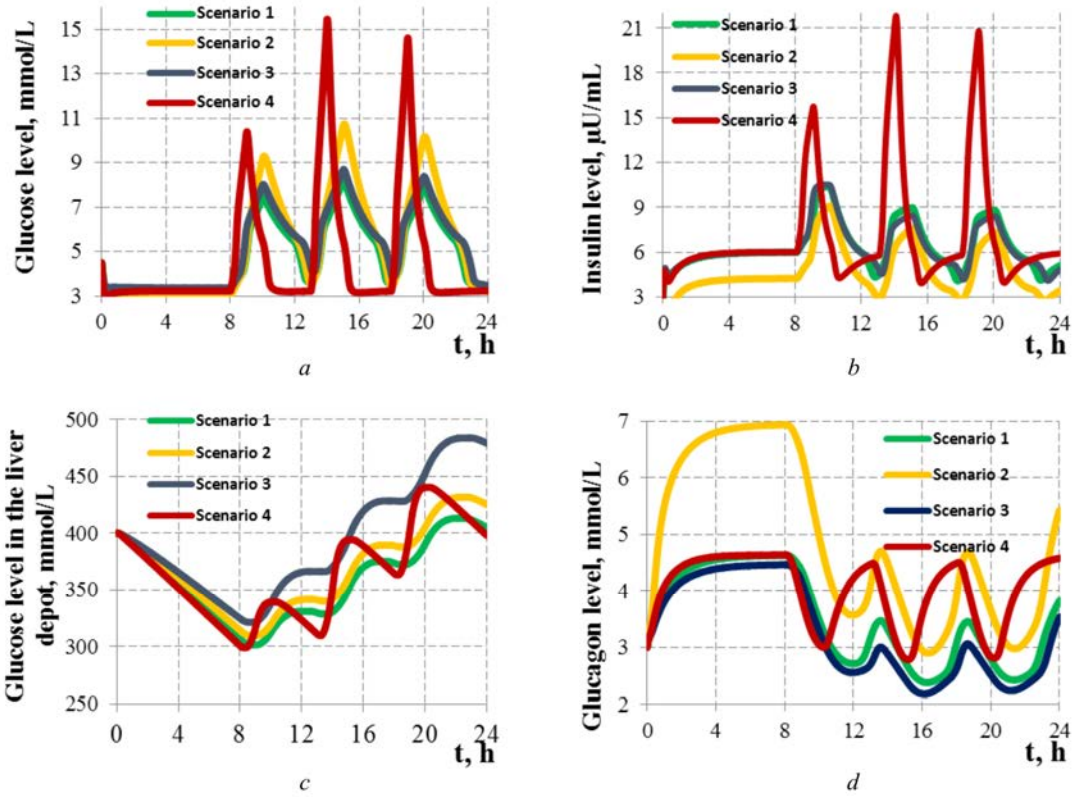

Figure 4. Numeric modeling results

Figure 4a provides comparison of the results obtained in four scenarios that describe glucose levels in dynamics. The peaks observed in the graphs correspond to meals. The glucose level reaches its maximum during lunch (approximately 1–2 p.m.), which corresponds to the peak in carbohydrate introduction from the GIT. Within the first scenario, blood glucose reaches 8.2 mmol/L and declines faster to its safe levels. Within the second scenario that involves modeling type 1 diabetes mellitus, the peak values are 10.8 mmol/L; within the third scenario, 8.8 mmol/L. In case of diabetes, periods when blood glucose is elevated (higher than 7 mmol/L) are longer as well as the glucose levels themselves are higher as compared to healthy people, which increases risks of concomitant diseases and complications. Within the fourth scenario, the peak glucose levels reach 15.5 mmol/L, which is considerably higher than in previous three scenarios. Although blood glucose grows for a shorter period of time, the obtained values are critical (above 11 mmol/L) and can induce considerable vascular damage. Therefore, introduction of slow carbs balanced over a day in first three scenarios ensures less considerable growth in blood glucose even in patients with diabetes. Imbalanced consumption of fast carbs, for example fast food, leads to very high blood glucose levels even in people without diabetes and even if carbohydrate consumption is within its recommended ranges. This is especially true if caloric contents are higher in one meal against others; such high blood glucose levels create elevated health risks. If patients with diabetes have such unhealthy imbalanced diets, a rise in blood glucose is going to be even higher and their health will surely be affected more seriously.

Figure 4b shows blood insulin dynamics. Within the first scenario, insulin production and effects are in equilibrium and blood insulin is within its safe ranges. In the scenario 2, the insulin level is considerably low, varies between 0.3 and 9 μU/mL and reacts to meals very

weakly. This state is typical for type 1 diabetes mellitus. In the third scenario, insulin production is not disrupted and the graph is practically the same as in the first scenario that describes a healthy person. Blood insulin reaches its peak, which is equal to approximately 10.6 μU/mL, in the third scenario (10.2 μU/mL in the first scenario), which corresponds to normal body reaction. Some rise in blood insulin is associated with the body trying to compensate for high blood sugar by producing more insulin than necessary within the third scenario. However, since cells are resistant to insulin, its impact turns out to be ineffective and blood sugar remains high. Within the fourth scenario, the insulin level also grows to 21.3 mmol/L as a response to higher blood sugar levels and this, in general, corresponds to an adequate reaction in a healthy body.

The Figure 4c shows how the glucose concentration changes in the liver (depot). In the first 8 hours (sleeping time), glucose flows from the liver into blood to maintain normal blood sugar levels. However, the situation starts to change between 9 a.m. and midnight and the glucose concentration grows in the liver. This happens because the liver actively stores up glucose as glycogen reacting to elevated blood sugar levels. After midnight, the glucose concentration in the liver stabilizes and returns to its initial level in the first and fourth scenarios. In this case, when functional disorders are absent in the body, the carbohydrate balance is observed. It should be noted that blood sugar is higher than its normal level in the second and third scenarios. Oversaturation with glucose makes the body start to deposit excessive glucose in the liver increasing the concentration in the depot by 25 mmol/L and 80 mmol/L in in the second and third scenarios respectively by the end of the day. The depot in the liver has certain accumulation limits and if the situation occurs every day, we can expect that excessive carbohydrates will start to transform into fats very soon thereby increasing obesity risks. A similar situation will develop even if functional disorders are absent in case the carbohydrate intake function $f(t)$ grows. In the fourth scenario, when dysfunctions are absent, the body manages to maintain the carbohydrate balance; in this case, high blood sugar is the only risk factor. Our analysis of the up-to-date literature data has shown that a high proportion of carbohydrates in a diet is a common reason for obesity, diabetes mellitus and associated cardiometabolic diseases. Obesity is most frequently associated exactly with type 2 diabetes mellitus, which confirms the obtained results as regards high stocks in the third scenario. Excessive carbs consumption induces endocrine deregulation characterized with hyperinsulinemia, which leads to energy division with growing fat mass deposits [21, 22]. Control over caloric contents in a diet and low sugar consumption authentically leads to declining prevalence of circulatory diseases and associated mortality in a population [23, 24].

The Figure 4d illustrates blood glucagon dynamics. In the first and third scenarios with normal insulin production, glucagon levels are practically identical varying between their minimum values of 2.2 mmol/L and maximum ones of 4.7 mmol/L during the day. In contrast, the second scenario describes a situation with considerably elevated blood glucagon levels reaching 6.9 mmol/L. When insulin is in deficit, glucagon production grows as a compensatory mechanism, which, in its turn, promotes hyperglycemia. In the fourth scenario, glucagon levels grow to 4.5 mmol/L due to a rapid decline in blood sugar levels and the necessity to stimulate glucose release from the liver. As any external sources of sugar are absent between midnight and 8 a.m., the solution to the system approaches its stationary state excluding the glucose concentration in the depot, which declines during this period. Blood glucagon levels decline after a meal, which is consistent with available literature data: in physiological conditions, glucose and insulin levels grow after a meal and glucagon levels decline evenly by 30–40 % of the basal level [25]. On the contrary, glucagon secretion grows steadily by 50–70 % during fasting.

This balanced regulation ensures maintaining stable blood sugar levels within their physiological ranges (4–5.5 mmol/L)[7] [26, 27].

This model can be used to predict individual health risks associated with blood sugar levels and a period of them exceeding physiological ranges in various diets (fast food, food with high caloric contents, and imbalanced daily diets). Depending on the simulation results, disease prevention measures can include optimal individual recommendations for balancing the amount of consumed carbohydrates and meals per day.

Conclusions. We have developed a new mathematical model that describes carbohydrate metabolism regulation and makes it possible to predict blood glucose levels as a major risk-inducing factor in various diets considering individual diseases of the gastrointestinal system. The results obtained by numeric modeling demonstrate that the glucose concentration is stable provided that metabolism is normal and slow carbs are consumed as a part of a balanced diet. They also show deviations from the physiological norm in patients with diabetes or due to consumption of fast carbs unbalanced over time thereby providing a better insight into dynamics of metabolic changes in the body.

The developed approaches can give grounds for further studies in the field and make for creating more effective measures to prevent diseases associated with disrupted carbohydrate metabolism and pancreatic diseases. In future studies, it is advisable to consider carbohydrate metabolism in combination with fat metabolism, which allows for more detailed consideration of pathways typical for diabetes and concomitant pathologies.

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