Modelling of the Blood Sugar Level with the Use of Genetic Algorithms

Marek Kamiński, Rafał Kotas, Paweł Marciniak, and Maciej Sałata

***Abstract*—This paper presents an example model of human body with particular focus on glucose level modeling designed for type 1 diabetes. The first part of the work describes motivation of the research, necessary simplifications of the model, parameters identification methods and implementation method. The second part is focused on an example examinations based on preliminary database of patients. It contains verification and evaluation of the presented model and plans of future work.**

***Index Terms*—glucose, glucose-insulin system, diabetes, blood glucose monitoring**

I. Introduction

NOWADAYS diabetes is one of the most common chronic, noncummunicable diseases in the world. According to WHO 2016 report on diabetes, 422 millions of adults were living with diabetes in 2014, rising from 4,7% to 8,5% of adult population. WHO estimates that diabetes would be the seventh of main causes of death in the world [4]. Taking into consideration only 2012 diabetes caused nearly 1,5 million deaths [4]. An economic issue is strongly connected with diabetes. It is estimated that the global cost of this particular disease in 2014 was 612 billion of dollars [10]. According to [5] in 2011 nearly 11% of total costs spent on health care were spent on diabetes treatment. Furthermore, as shown in Table I number of deaths (for 10,000 inhabitants) associated with diabetes is growing over the years.

TABLE I
THE NUMBER OF DEATHS ASSOCIATED WITH DIABETES FOR 10 THOUSAND INHABITANTS IN POLAND [9]

1980	1990	2000	2010	2013
1.3	1.5	1.4	1.7	1.9

One of the most important aspects of this disease is how much its treatment impacts patient life. However frequent blood tests and insulin injections prevent from devastating effects of this disease. One of the most absorbing issue for diabetics is that both low blood sugar (hypoglycemia) and high blood sugar (hyperglycemia) is very dangerous.

Uncontrolled blood sugar level leads to decrease in patient life standard. Moreover even if the patient controls his glucose level, it is usually not efficient enough and still leads to complications [6]. The reasons for this are both not taking seriously health condition as well as (in some cases) not understanding the mechanisms of human organism responsible for proper blood sugar management and not following the doctor's recommendations [6]. The real glucose level during the day is rarely known due to the fact that diabetic patients controls blood sugar level only a few times a day [8]. Only after few minutes after each test it could be assumed that the sugar level is precisely known.

However the later from the blood sugar test the more the actual glucose level differs. Obviously you can speculate with a high probability that the carbohydrate-containing meal will increase blood sugar level, and vice versa, the injection of insulin will decrease it. Nevertheless both of these activities are carried out in small distance of time and because of this it is usually very hard to determine (without measurement) what is the current glucose level. It is illustrated as non-deterministic state machine in Figure 1.

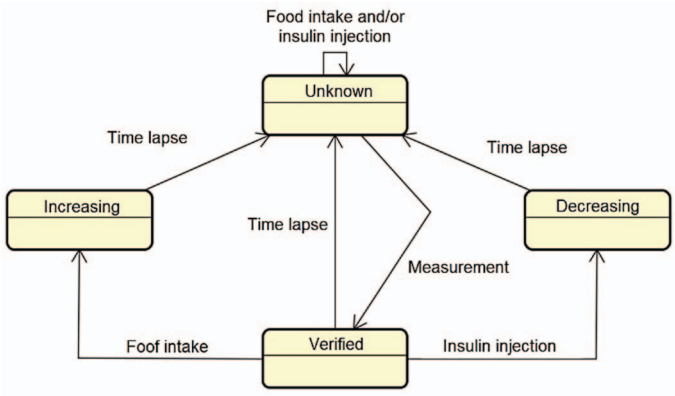

Fig. 1. State diagram of blood glucose levels in diabetes patients.

II. Main Assumptions of the Model

The aim of the article was to present the method of model parameters selection. The authors did not make any changes in the model of blood glucose alone, so they decided not to refer to existing models. The model of glucose-insulin system was proposed by Stolwijk and Hardy in 1974 [1,2]. It was modified by Tolic et al. in 2000 [3]. It consists of two differential equations describing the change in blood sugar and insulin levels:

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$$\frac{dg}{dt} = \begin{cases} \omega - vgi - \lambda g - \mu(g - \Theta) + G(t), g > \Theta \\ \omega - vgi - \lambda g + G(t), g \le \Theta \end{cases} \quad (1)$$

$$\frac{di}{dt} = \begin{cases} -\alpha i + I(t) + \beta(g - \Psi), g > \Theta \\ -\alpha i + I(t), g \le \Theta \end{cases} \quad (2)$$

where:

g glucose concentration;
i insulin concentration;
G(t) glucose delivery (associated with meals);
I(t) insulin delivery (associated with injections);
α proportionality factor associated with the removal of the insulin from blood;
β proportionality factor associated with the production of insulin by the pancreas depending on the glucose concentration;
ω conversion of the glucose–glucagon proportionality factor;
λ proportionality factor associated with the removal of glucose from the blood unrelated to the action of insulin (eg. brain cells);
v proportionality factor associated with the removal of glucose by the action of insulin;
Θ, ψ Threshold glucose concentration;
μ proportionality factor associated with the release of glucose into the blood (eg. liver).

The model described in this article is dedicated to patients with diabetes type 1. Basic simplification was applied, which was based on assuming β = 0 (no insulin production by the body). Because there was no way of measuring blood insulin levels, this part of the equation was not solved openly, but the associated components of insulin withdrawal and injection were included in equation no 1. This paper is focused on modelling of glucose level.

There are two main assumptions of the our model. Both glucose assimilation of food and insulin absorption can be calculated for each patient as a relatively simple functions, mainly dependent upon the timing and quantity of substances assuming their superposition. In addition, a single parameter describing the glucose changes in the blood (not connected with insulin influence) has been entered. The simulation of a particular model is performed with the use of extrapolation Euler method. It was chosen due to its computational simplicity. The fact that this method is characterized by generally low convergence is compensated by modelling only slowly changing processes.

- The data gathered by the system correspond to the most standard data collected by the patient during a normal day. Patient records the following information:
- Measurement of blood sugar level (date of the measurement and the result is given in mg / dl);
- Meals eaten during the day. (Date of consumption and the equivalent of a carbohydrate in IU);

Injections of insulin (date of injection, type of injected insulin, and the amount given in IU).

The main disadvantage of the model is its highly specific character for each modelled organism. Each person has an individual set of parameters used in the equations describing the model. In order to determine these parameters, the following procedure was adopted:

- Gathering experimental data from the period of several months (for a particular patient).
- Construction of a model using optimization methods (selected genetic algorithms). The difference between the results of simulation using the model and collected experimental data was defined as an objective function. All of the model parameters can be changed.
- Selection of a model giving the results that are closest to the reality.
- Using the model as a predictor of blood sugar level under constant conditions of life.

Presented research was conducted with the help of patients whose health state does not change rapidly and whose diabetes is considered to be stable. During the process of data collection patients should not undergo any surgeries and also their diet and social situation should not be subject to rapid changes. The analysis includes patients with type 1 diabetes.

Patients with type 1 diabetes have damaged β-cells of the islets of Langerhans, which are located in the pancreas. Because they are the only cells in the human body able to produce insulin, the patient has completely disrupted this hormone economy [11]. Diabetics with type 1 diabetes are dependent on insulin injections. Their pancreas do not produce the insulin at all (or produce at a negligible level) and thus they cannot respond to the rise of blood sugar level after a meal.

Type 2 diabetes is the more common disease. In diabetics both synthesis and secretion of insulin is impaired [12]. Designed application could be also used for patients with type 2 diabetes, but it requires an extended model. At least it should be enhanced by the amount of insulin produced by patients pancreas that depend on the glucose level.

III. Methodology

The choice of genetic algorithm was not dictated by any particular requirements of the optimized problem. It was dictated by the authors experience of the above-mentioned algorithm, no equation of error function and no restrictive requirement for the effectiveness of the solution. In addition, the genetic algorithm gives a better chance of finding a global minimum than deterministic algorithms.

A genetic algorithm optimizes the 28 variables shown in Figure 2:

- 3 sets of 9 variables describing each function (a, b, c), where:
  - Δx1 – Δx4 is the distance between successive points on the x-axis which changes the angle of the slope parameter relative to the x-axis. Range for each variable is [0, 1];
  - α1 – α3 describe the slopes of a linear functions relative to the axis OX. The value of α0 is always equal to zero because this fragment simulates delay in the absorption of carbohydrates / insulin. The other coefficients are subjected to optimization. Their ranges are [0,8];

- multiplier - this is the factor responsible for scaling the function (relative to the axis OY). It is also the largest value obtained by the function. The value of a multiplier coefficient ranges between 0 and 100. It is expressed in mg/dl;
- influenceTime - this is the factor responsible for scaling the function (relative to the axis OX). It is also the maximum time of function influence. It is expressed in minutes and the range for this coefficient is [0, 2048];

- last optimized variable is a constant indicating a change in blood sugar levels in time. It ranges from -10 to 10, and its unit is mg / dl / hr. (D)

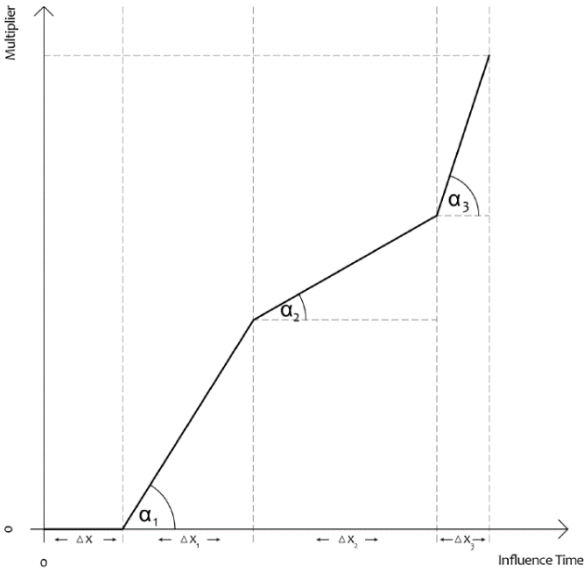

Fig. 2. Description of the variables involved in the genetic optimization algorithm.

In the paper it is assumed that the model of the patient can be determined by:

a) piecewise linear function describing the absorption of insulin type R
b) piecewise linear function describing the absorption of insulin type N
c) piecewise linear function describing a change in blood glucose levels after a meal
d) constant rate of glucose level change per unit of time.

Each of the functions a), b) and c) is a combination of four linear functions. All of them have defined domain and codomain. Each function is described by 9 parameters. A graphical presentation of the function examples is shown in Figure 3.

IV. Application

The application was divided into several modules and includes components such as: Frontend - used to generate views for user and Backend – used for data operations. A block diagram of an application is shown in Figure 4.

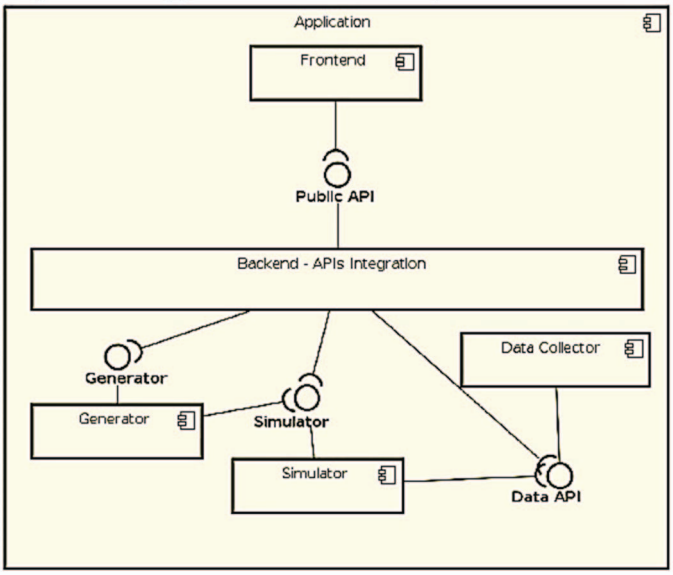

Fig. 4. Block diagram of an application.

These two modules communicate using RESTful protocol. The data is exchanged using JSON. Backend monitors the three underlying components of the application and coordinates the execution of source code. The entire application uses a code generator standard, called jHipster.

Backend module is based on the Spring Framework. The application relies on its dependency injection mechanism. In addition, other components from the Spring Framework have been used. Logging is based on Spring Security. Access layer to the database has been implemented basing on the Spring Data project. Data exchange is facilitated by using Spring Web module that significantly accelerates the creation of access points of RESTful protocol, using the communication format JSON.

Frontend module is based on the framework AngularJS first generation. It is written in JavaScript. Therefore, the generation of the appearance of the displayed data is performed on the user side. Framework works with HTML5 and design pattern of dependency injection, which greatly improves the management and maintenance of the resulting code [7]. It is also the only framework to generate a view that is supported by jHipster.

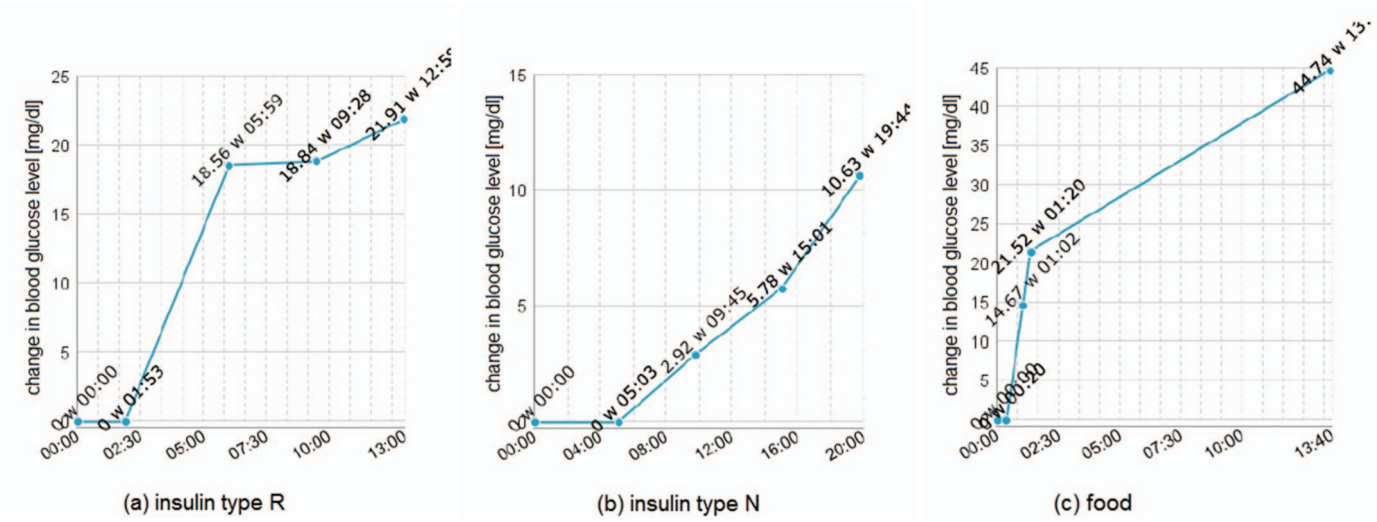

Fig. 3. Examples of functions of assimilation model.

An essential element of user interface are charts (generated by the application). They present the measurements, simulation results, adopted carbohydrates exchanges and insulin injections. An example of the simulation is shown in Figure 5. The following data are presented in this figure:

- red bars - adopted units of carbohydrate exchanges;
- blue bars - mapping of amount of injected insulin units;
- orange dotted line - the actual measurements of a patient [mg/dl];
- green line - simulation model measurements calculated by the application [mg/dl].

The closer green line is to orange dashed line, the better result is achieved.

The Y-axis on the left refers to the food consumed and units of injected insulin. The Y-axis on the right refers to the measurement of glucose concentration in blood. OX axis contains the date (month, day, hour and minute) when the events described above took place.

V. Results

The study included so far two patients previously diagnosed with type 1 diabetes:

- patient no 1 - male, year of birth 2000, disease: type 1 diabetes, date of diagnosis: 09.2014;
- patient no 2 - female, year of birth 1985, disease: type 1 diabetes, date of diagnosis: 1998.

VI. Summary

This paper describes the modelling of the human body based on a simulation of changes in the quantities of each selected substance under the influence of certain external factors. Coefficients used in the model, describing the changes, of course, cannot be determined or calculated. Moreover, for each patient, the value of these coefficients is probably a little different. The approach of optimization determination of these values based on historical data seems to be justified. As it is shown in Figures 9 and 13 the model has the predictive features of blood glucose levels for the tested subjects. The model is not perfect, of course, but it seems that it could serve as a coarse tool that allows the type 1 diabetic to assess the behaviour of one's own body. Table II presents the mean squared error (MSE) for obtained results.

TABLE II
Mean squared error (MSE) for obtained results.

	Model	MSE	MSE/no of samples
Patient no1	Nonoptimized model	4550	59.10
	Optimized model	3284	42.65
	Prediction ability model	399	36.29
Patient no2	Nonoptimized model	7142	39.24
	Optimized model	6075	33.38
	Prediction ability model	441	12.33

The application has further development potential. Collecting information about diabetes is very valuable. There is only one Polish web page showing the functionality of a paper diary of self-control. It is the http://dzienniczek.diabetescare.bayer.com.pl, which was created during the development of this study (July 2015). An important direction of the application development, should be to extend its functionality also for patients with type 2 diabetes. This would significantly expand the group of recipients. However, this would require development of a blood sugar disappearance model under the influence of exercise. It is a matter of further research and development.

Another direction of the application development may be an attempt to model the other chemical processes in human body. Monitoring body weight (not necessarily for diabetics) seems to be the most interesting and perspective. A way to solve the problem would be almost analogous with simulation of a blood sugar level. It would also require an analysis of many parameters with values optimized basing on historical data.

Fig. 5. Example plot of simulation generated by application.[1]

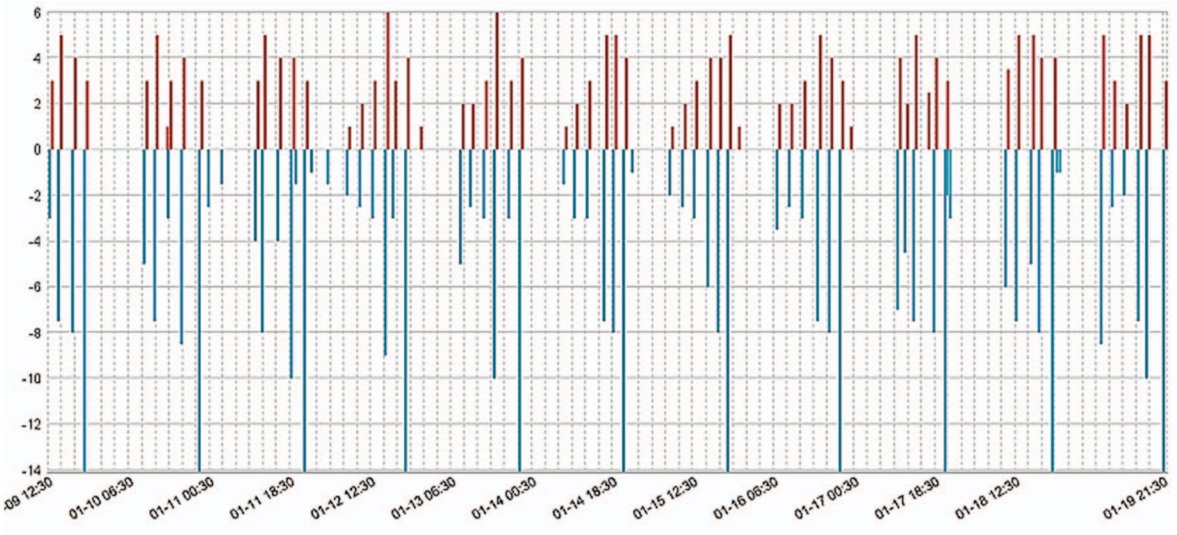

Fig. 6. Food intakes and insulin injections for patient no 1.[1]

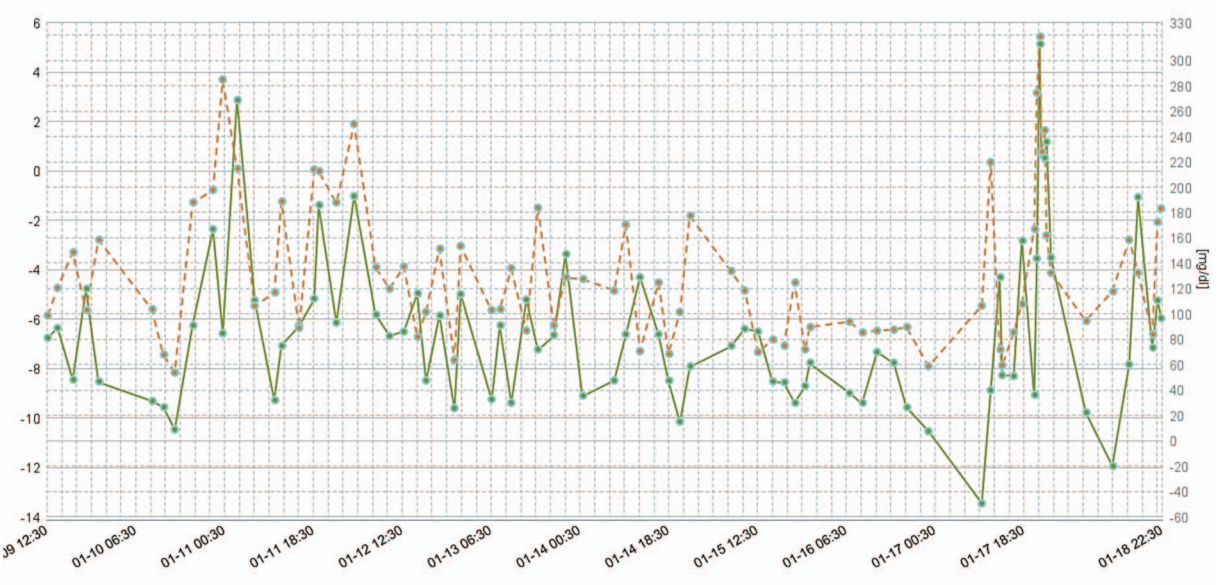

Fig. 7. Measured course of changes in blood sugar levels and the results of nonoptimized model for patient no 1.[1]

[1] The charts legend is located at the end of the chapter 4.

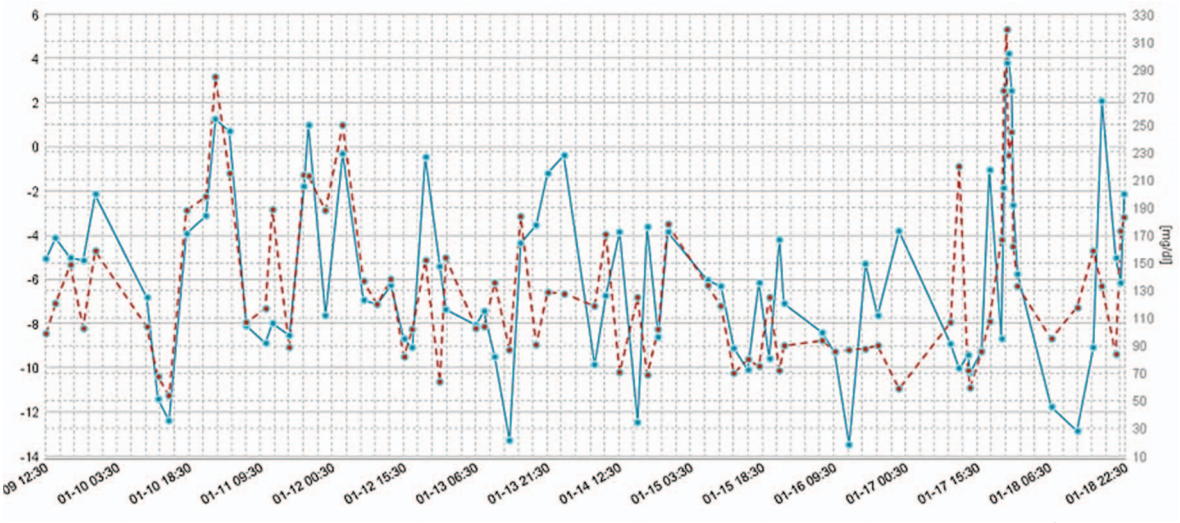

Fig. 8. Measured course of changes in blood sugar levels and the results of optimized model for patient no 1.[2]

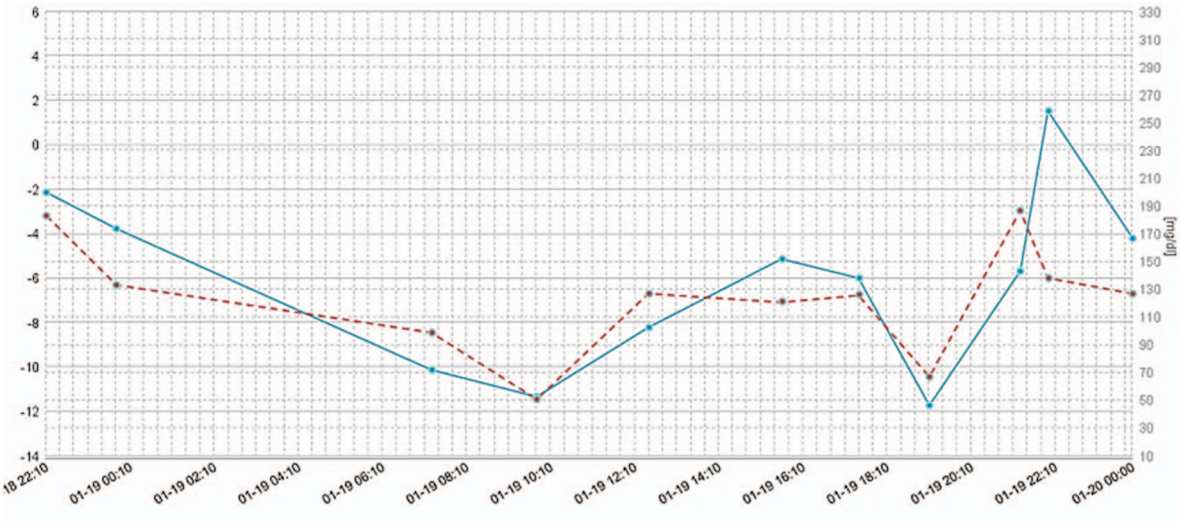

Fig. 9. The predictive ability of the model for further observation time for patient no 1.[2]

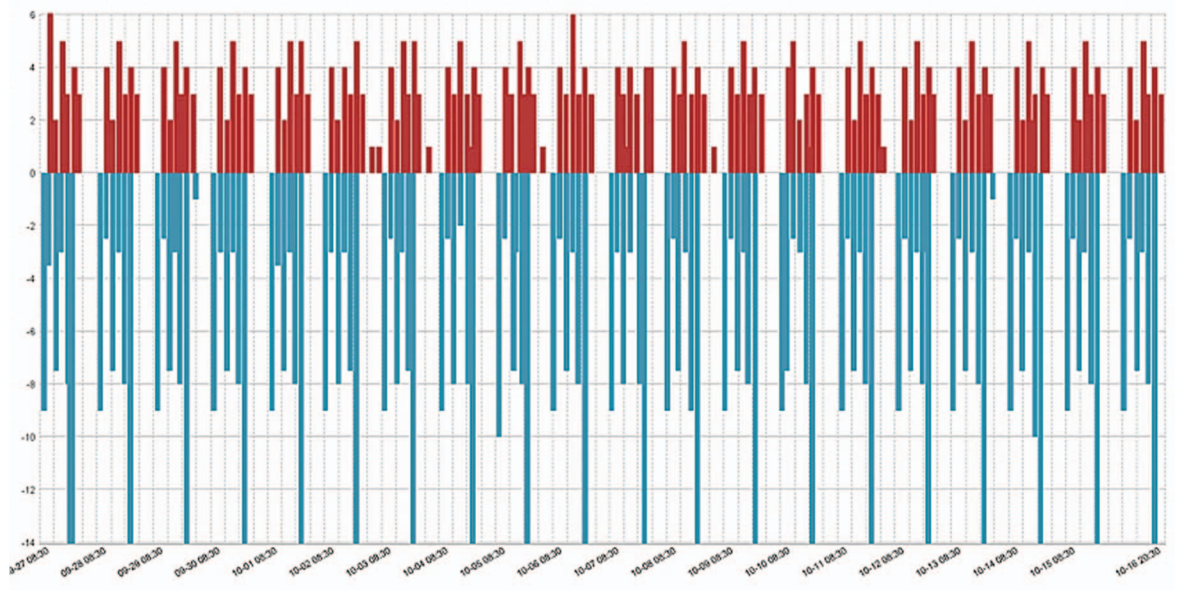

Fig. 10. Food intakes and insulin injections for patient no 2.[2]

[2] The charts legend is located at the end of the chapter 4.

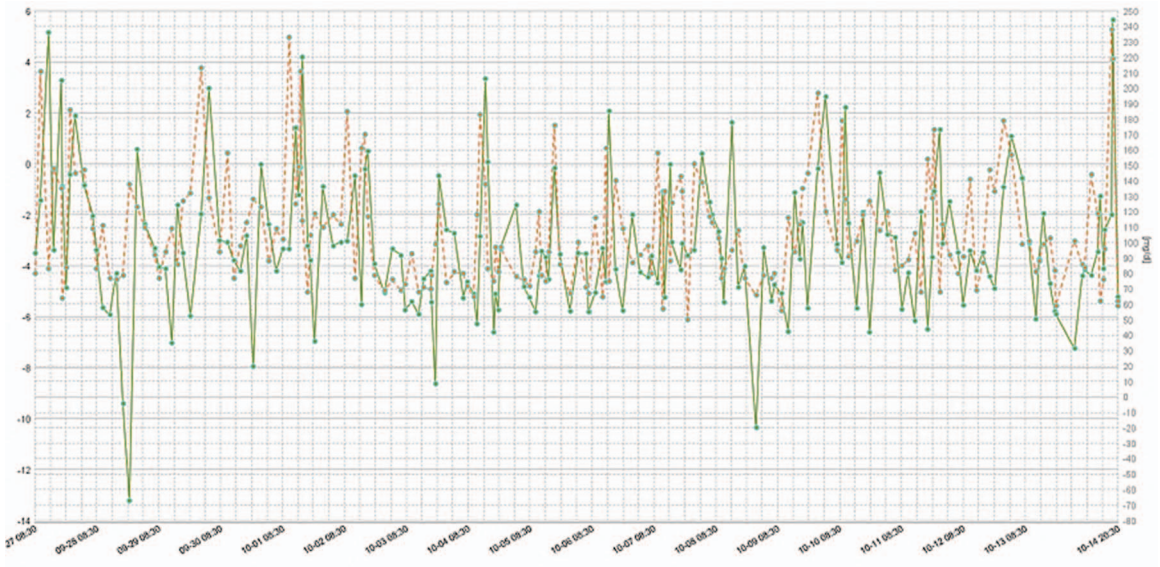

Fig. 11. Measured course of changes in blood sugar levels and the results of nonoptimized model for patient no 2.[3]

Fig. 12. Measured course of changes in blood sugar levels and the results of optimized model for patient no 2.[3]

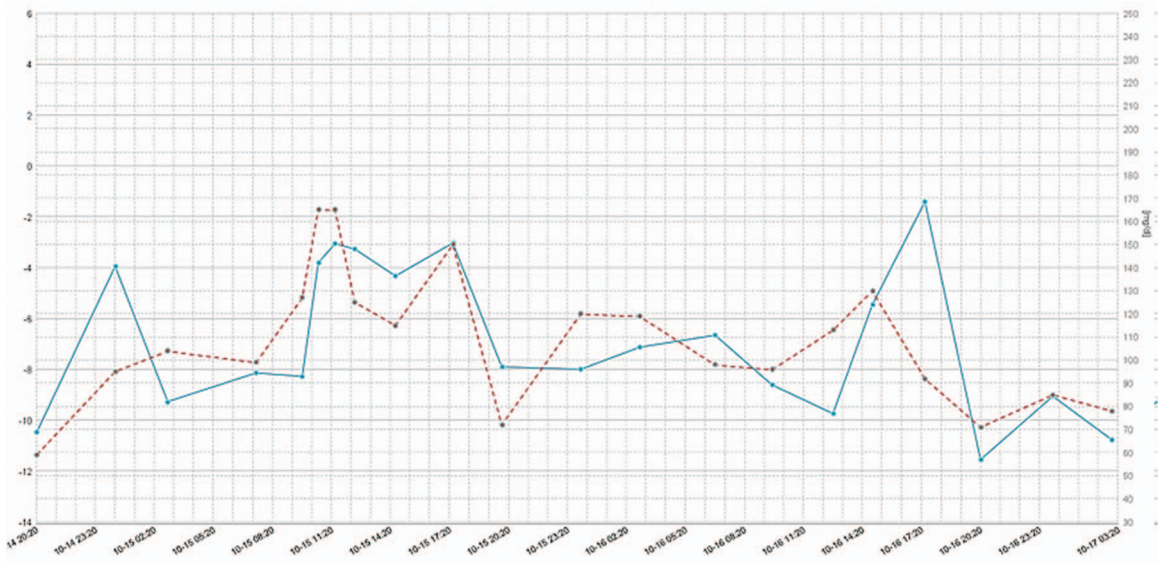

Fig. 13. The predictive ability of the model for further observation time for patient no 2.[3]

[3] The charts legend is located at the end of the chapter 4.

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