

Diabetes Lifestyle Support with Improved Glycemia Prediction Algorithm

Peter Gyuk¹, Tamas Lorincz², Rebaz A. H. Karim³, Istvan Vassanyi⁴

Medical Informatics R&D Center

University of Pannonia

Veszprém, Hungary

e-mail:¹peter.gyuk@virt.uni-pannon.hu, ²tamas.lorincz@virt.uni-pannon.hu, ³rebaz.ahkarim@virt.uni-pannon.hu, ⁴vassanyi@almos.vein.hu

Abstract— This paper proposes a combined model to predict the blood glucose level of people with diabetes. Our method consists of two efficient models found in literature and takes nutrition, applied insulin, and initial glucose level into account during the calculations. An extension has been made to these models using various model training methods. Our aim is to help diabetics calculate the insulin need with this efficient algorithm later implemented in a user-friendly software. The tests, that are based on real data, show a significant improvement in the results if model training methods such as Genetic Algorithm (GA) is used. On the other hand, the numbers reveal the weaknesses of our method, which has to be fixed in the future. During an all-day validation, the prediction error was smaller than 3 mmol/l in 83% of the cases while using GA. Compared to other tests found in literature our model seems to be a good start in predicting glycemia, but needs further improvements.

Keywords—Glucose-level tracking; eHealth; Genetic algorithm; Glucose-Insulin system; Glucose absorption; Diabetes mellitus; Outpatient care

I. INTRODUCTION

Diabetes mellitus is a crucial problem in modern healthcare, since 8% of the population has diabetes in the target age (20-79), according to a recent survey [1]. Furthermore, the number of diabetics may increase by 50% within 2 decades [1]. These numbers remind us of the importance of treating diabetics. Our aim is to provide a tool for them with the help of modern technology and improved prediction algorithms. In case of success, our method can be easily implemented as an add-on to a mobile lifestyle logging application that can be used by many patients to calculate their insulin need.

The basic motivation of our efforts is to create a tool that diabetics can use in everyday life to calculate their blood glucose levels. To accomplish this, a reliable method has to be developed to predict the glycemia based on the lifestyle and medication log of the outpatients. Our previous work [2][3] showed that the models we chose are capable of a 1-3 hour prediction, but corrections are required to avoid excessive over- and under-estimations. As we reached slightly satisfactory results for the long term (4 or 6 hours) prediction, we started to focus on the model training methods to create better outcomes. There are a lot of methods to be investigated, such as: neural network, fuzzy logic, least square method and genetic algorithm. Some of these have already been applied to the problem of blood glucose

prediction [4-12]. In the next subsection we give an overview of the current results.

A. Literature Overview

There are several models available for Blood Glucose Level (BGL) prediction. Most approaches are based on a combination of these models. We review those that include validation on realistic data.

The system demonstrated by Stahl et al. [4] consists of three main parts: Glucose Sub-Model, Insulin Sub-Model and the Glucose/Insulin Interaction Model. These three parts are modeled separately using compartment models and linear black-box models [5][6]. During a 6 months period, input data was collected from a patient diagnosed with Type 1 Diabetes (T1D). Meals, insulin injections and glucose measurements were logged. Researchers had difficulties reaching prediction error smaller than 1 mmol/l in 95% of the cases with 2-hour-ahead prediction.

Robertson et al. [7] used Elman's recurrent Artificial Neural Network (ANN), which predicts BGL based on the history of BGLs, meal intakes and insulin injections. BGL history came from the freeware mathematical diabetes simulator named AIDA (Automated Insulin Dosage Advisor). The data set consisted of 28 days and 2688 values. The ANN was trained using all available BGL data for short-term prediction (up to 1 hour). For long-term prediction the ANN was trained with input vector events. Input vector events included 2 meals, 2 short-acting insulin doses, and 2 long-acting insulin doses a day. The maximum error for blood glucose prediction was 0.27 mmol/l for short-term predictions (15, 30, 45 and 60 minutes), 0.2 mmol/l for the 8-hour, and 0.36 mmol/l for the 10-hour predictions, respectively. These are impressive results, however, we must keep in mind that the validation base was a mathematical diabetes simulator data set. In contrast, we used real life measurements of humans.

Shanthi et al. [8] carried out the prediction of blood glucose with a simple neural network model, which was trained with the assistance of extracted features. They used a novel feature based prediction algorithm for forecasting the blood glucose values ahead of time. The data set was obtained from diabetic patients in a hospital setting with different insulin therapies using Medtronic Continuous Glucose Monitoring System (CGMS). The average errors of this approach are 0.55 mmol/l for the 30 minutes prediction, 0.83 mmol/l for 45, and 1.11 mmol/l for 60 minutes prediction, respectively. These results are promising, but the

validation data was highly controlled, and 50% of data was used for training. In contrast, we used 30% of data for model training with less controlled outpatient data.

The sole aim of the Plis et al. [9] study is hypoglycemia prediction. To perform this, they used the Support Vector Regression (SVR) model with physiological features. Instead of tuning parameters, which differ among patients, they used state variables to create features for the SVR model that was individualized for each patient. An extended Kalman filter was run using the training/test points. Input data were collected from 5 T1D patients. The average errors for SVR are 1.25 mmol/l for 30 minutes and 1.99 mmol/l for 60 minutes. This can be a good comparison base to our results.

There are also other recent approaches not so close to the focus of this paper. Chuah et al. [10], used non-invasive, i.e., less reliable blood glucose concentration measurement including healthy volunteers. Seizabourou et al. [11] also used a realistic data set for validation and reached promising results, but without taking meals into account. Liszka [12] used the hybrid Artificial Intelligence technique, which combines the principal component method and the neural networks. However, the authors estimated blood glucose levels only two times a day, while we estimate every 5 minutes.

The rest of the paper introduces our model, the validation method, and the results. Section II includes a short overview of our model and presents the model training methods. Section III reviews our testing phases followed by the results and the discussion detailed in Section IV. Section V is a short overview of our software that is developed to support the test process. Finally, Section VI concludes the paper and outlines future works.

II. METHOD

A. Model

We created a combined model which reflects the real process happening in our body. Following metabolism, we split the whole procedure in two parts. One of them is insulin absorption, which is simulated with differential equations:

$$\frac{dG}{dt} = -K_{xgi}G(t)I(t) + \frac{T_{GH}}{V_G} \quad (1)$$

$$\frac{dI}{dt} = -K_{xi}I(t) + \frac{T_{iGmax}}{V_I} f(G(t - \tau_G)) + \frac{1}{V_I t_{max,I}} S_2(t) \quad (2)$$

$$\frac{dS_2}{dt} = \frac{1}{t_{max,I}} S_1(t) - \frac{1}{t_{max,I}} S_2(t) \quad (3)$$

$$\frac{dS_1}{dt} = -\frac{1}{t_{max,I}} S_1(t) - u(t) \quad (4)$$

The first equation calculates the blood glucose level (G), depending on insulin absorption (I), calculated by (2). This model includes two subcutaneous insulin depots (S_2 and S_1) described by (3) and (4). These depots simulate subcutaneous insulin absorption. For further details of this model and the parameters see [13][14] and Table 1.

The second part of our combined model describes the glucose absorption from meals [15]. It is a two-compartment model based on mass balance equations. As Figure 1 shows, it divides the digestion into two parts; stomach and intestine. The model takes protein, lipid, monosaccharide, fiber, and starch intake as input, with each one having its own effect during the absorption. This method can deal with mixed meals with components of different Glycemic Indices [16] and takes into account the effect of fiber. Moreover, digestion overlap between two consecutive meals is handled properly. For more details about the model and the parameters see [17].

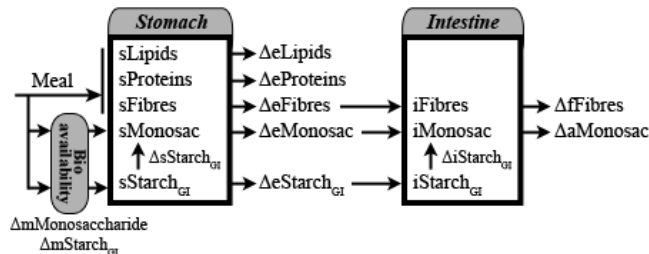


Figure 1. The process of absorption from mixed meals

The combination of these two models can support diabetics, using subcutaneous insulin injections, no matter if they have Type 1 or Type 2 diabetes [18]. The algorithm properly handles insulin and meal absorption overlaps, as for a longer-time prediction (6-8 hours), the absorption of the insulin and the glucose from food could be in progress during the next meal.

B. Parameter Identification Algorithms

We chose models with large parameter sets, which simulate the real life process efficiently. In the current phase of work, the parameters of the glucose absorption model is generalized for all patients, but these parameters should be investigated later as well. On the other hand, the parameters for the glucose control system are different for each diabetic. Some of these parameters can be measured by an intravenous glucose tolerance test [19], but is too complicated to be made for each person in a realistic outpatient setting. This is the main reason why we need model training methods.

TABLE I. MODEL SENSIBILITY TEST (RESULTS IN DESCENDING SENSIBILITY ORDER)

Parameter	Change % in results with the given parameter change %			Order
	5 %	50 %	200 %	
V_i (insulin distribution)	5.46	50.23	145.09	1.
K_{xgi} (glucose uptake rate)	5.27	37.45	71.46	2.
K_{xi} (insulin disappearance)	2.25	22.38	82.57	3.
T_{gh} (glucose uptake balance)	0.27	2.71	10.92	4.
V_g (glucose distribution)	0.26	1.80	3.61	5.
T_{iGmax} (insulin release)	0.07	0.74	2.91	6.
τ_G (insulin release delay)	0.01	0.08	0.33	7.

The running time of the training algorithms depends on the number of the parameters to be trained. As the glucose control model has many variables, a model sensibility test was made to narrow the parameter set (Table I). This means that the training algorithm can run within the same time with fewer parameters to be trained and a wider search range. The results of this test showed that there are 3 parameters which have a significantly larger effect on the results than the others: K_{xi} (disappearance rate for insulin), K_{xgi} (glucose uptake by insulin-dependent tissues), and V_i (distribution volume for insulin). Thus we concentrated on these 3 parameters in the current phase, and they were trained with the methods as described below. For the other parameters, we used an average value suggested by the literature [14].

Two parameter identification algorithms were used. The first one is the Brute Force Algorithm (BFA) [20], which means a full search of parameters in a specific range. BFA analyzes all possible parameter sets within a specific range with the given stepsize. It is not optimal as the stepsize can be decreased ad infinitum, but the returned parameter values are almost perfect. The advantage of this method is its completeness, the disadvantage is the long running time.

The other method is the Genetic Algorithm (GA) [21]. GA simulates the process of natural evolution, using the tools of genetics like mutation and crossover. We used an open source library called GALib [22] in a simple genetic algorithm with one point crossover. The fitness function of the GA was the sum of the differences between measured and estimated blood glucose levels.

These training methods themselves have several parameters, henceforth, we performed a test to find the best parameterization. We used 3 data sets including both Type 1 and Type 2 patients. Tables II and III show the results. The best BFA setting was BFA 6, where the stepsize was 0.5, the finding range was 3, and the average running time was 35 seconds. In GA's case, we chose the GA 6 parameterization with the population size of 40, the generation number of 20, the mutation probability of 50%, and the crossover probability of 90%. The high chance of mutation means a more stochastic algorithm. GA 1 was also used during the tests, with the population and the generation of 10, the mutation of 1%, and the crossover of 90%.

TABLE II. BRUTE FORCE ALGORITHM PARAMETER TEST BASED ON TOTAL DIFFERENCE IN MMOL/L

Data set	Base	BFA 1	BFA 2	BFA 3	BFA 4	BFA 5	BFA 6
D1	13.51	9.545	9.33	13.32	10.82	11.68	9.33
A1	177.94	171.65	161.80	155.41	155.41	159.09	146.26
B1	799.94	417.78	372.76	459.49	375.46	375.29	375.29

TABLE III. GENETIC ALGORITHM PARAMETER TEST BASED ON TOTAL DIFFERENCE IN MMOL/L

Data set	Base	GA 1	GA 2	GA 3	GA 4	GA 5	GA 6
D2	13.97	10.19	9.65	9.67	9.32	9.28	9.18
A2	552.90	430.37	430.99	419.86	417.71	415.57	415.66
B2	600.34	197.84	210.49	208.38	200.37	198.29	196.41

III. MODEL VALIDATION

The purpose of the validation is to test the prediction power of our algorithm. Accordingly, we used real life data from both type 1 and type 2 diabetics. We expected a significant improvement due to model individualization compared to our previous test using literature parameters [14]. The following subsections review the input data and the validation method.

A. Data Sets

During the tests, we focused on outpatients treated with subcutaneous insulin injections, which means ca. 26% of diabetics [23]. We had 7 different data sets of 5 persons, each one including at least 3 days of logging and 12 meals. We had a total of 101 meals and 24 days of input data. As Table IV shows, there were 3 Type 1 (T1D) and 4 Type 2 Diabetes (T2D) data sets. Four of the patients used the Medtronic CGMS and one of them (D) used an ordinary blood glucose meter. All 7 logs consist of insulin doses, meals, and blood glucose levels. A professional dietitian calculated the nutrient values for each meal using the hand written logs. Data sets A, B, and C are from the same patient in a controlled experiment, in which the meals were logged rigorously. This patient avoided any sport activities during the monitoring period. In contrast, for the Type 2 patients the meal log may contain inaccurate values as they were cured in hospital to adjust their inordinate glycemia and it was not possible to control if they consumed the same meals as offered in the menu. Moreover, sports were also compiled in their log, making the estimations more prone to error because currently the model can not handle this factor.

TABLE IV. INPUT DATAS

Data set	Type	Age	Insulin	Measure	Meals	Days
A	T1D	21	Apidra	CGMS	15	3
B	T1D	21	Apidra	CGMS	14	3
C	T1D	21	Apidra	CGMS	15	3
D	T2D	62	Humulin R	ordinary	15	6
E	T2D	78	Humalog	CGMS	14	3
F	T2D	61	Humulin R	CGMS	12	3
G	T2D	65	Humulin R	CGMS	16	3

B. Validation Process

The validation process consists of 3 phases. The first phase is the study of the model with parameters found in the literature [14]. We made meal wise tests, where the meals were treated as separate tests. This means zero startup blood insulin level and the model starts without any glucose absorption. In this phase, 2 hour, 4 hour, and 6 hour meal-wise tests were made to measure the correctness of the model in short-term and in long-term as well. We also made daily tests; one without model restarting and one with model restarting. This means that the estimated blood glucose levels have been set back to the measured value before each meal. This approach is a transition between meal-wise and daily tests, because the insulin and glucose absorption calculations

are continuous, but the blood glucose levels are corrected to avoid stacked errors.

In the second phase, we performed model training, i.e., parameter identification. We made whole day tests with restart using the brute force method and the genetic algorithm according to the model training parameter tests is Tables II and III.

In the third phase, we restricted the training data used for the parameter identification to a single day of the log and we used the rest of the log to validate the model with the estimated parameters. We performed all tests mentioned above. Using only a part of the input data for training and the rest for validation avoids over-training and simulates the planned real application of the model in a lifestyle support software tool.

IV. RESULTS

The results were divided in two categories; all patients and controlled data sets. The first one is a simulation closer to reality, while the second highlights the changes in the model as it contains less false data. Test phase 1 (Table V) clearly shows these differences, because in the case of controlled data sets the results were ca. 20% better on average. This improvement for the good of the controlled measurement is caused by the more precise logging. We can also see that longer the time after the meals, the higher the error between measured and estimated blood glucose level. The all-day tests with restarts show a significant improvement in all of the results and the maximum error is also decreased by at least 3 mmol/l. Also, 62% of the errors were within a 3 mmol/l range, which is a promising result for a whole day measurement. This number is even higher (76%) in the case of controlled measurement.

TABLE V. TEST PHASE 1: DEFAULT PARAMETERS WITHOUT ANY MODEL TRAINING, AVERAGE VALUES IN MMOL/L (MM)

All patients	Meal wise			Whole day		
	2h	4h	6h	No restart	Restart	
Average error	5.05	7.92	9.28	4.2	3.3	
Max error	10.62	14.93	17.25	10.34	7.31	
Ratio of error	< 1mM	34 %	24 %	21 %	22 %	32 %
	< 3mM	52 %	43 %	40 %	50 %	62 %
Controlled (A,B,C)	Meal wise			Whole day		
	2h	4h	6h	No restart	Restart	
Average error	4.26	5.26	5.45	2.5	1.88	
Max error	8.1	10.04	11.08	6.94	5.45	
Ratio of error	< 1mM	34 %	26 %	23 %	29 %	37 %
	< 3mM	56 %	51 %	52 %	65 %	76 %

The “Brute Force” caption in Table VI means the BFA 6 parameterization, described in Section III. “Genetic Algorithm 1” means GA 6 and “Genetic Algorithm 2” means GA 1. With model training, the results show a nearly 25% improvement in average error, but the maximum error almost remained almost the same when model restarting was

applied. With the brute force method, we could reach a ratio 50% for the errors within 1 mmol/l. This means that during a whole day half of the estimated values were in the error range of the measurement devices, i.e., 1 mmol/l, so they can be stated as perfect predictions.

TABLE VI. TEST PHASE 2: WHOLE DAY TEST WITH RESTART USING MODEL TRAINING, AVERAGE VALUES IN MM

All patients		Brute Force	Genetic Algorithm 1	Genetic Algorithm 2
Average error		1.81	2.18	2.54
Max error		5.83	6.8	7.82
Ratio of error	< 1mM	48 %	42 %	40 %
	< 3mM	79 %	73 %	71 %
Controlled (A,B,C)		Brute Force	Genetic Algorithm 1	Genetic Algorithm 2
Average error		1.51	1.64	1.68
Max error		5.24	5.49	5.64
Ratio of error	< 1mM	49 %	44 %	43 %
	< 3mM	86 %	83 %	83 %

The reason why model training on whole day tests have not been made is that we tried to create a real life simulation during test phase 3, where the calculated parameters were tested with the meal wise method. According to our proposal, the future software will make a parameter identification from a few days data flow and will estimate the blood glucose levels after each meal with the calculated parameters. To see how accurate this method is we used BFA 6 and GA 6 to estimate the parameters. Table VII shows the differences in the results to the default parameters. The improvement is not as significant as in Phase 2, but we can see 5% improvement in average error for GA 6 and an average of 10% for BFA 6.

TABLE VII. TEST PHASE 3: REAL USAGE VALIDATION FOR CONTROLLED TESTS, AVERAGE VALUES IN MM

Meal wise test (1 h / 2 h / 4 h)		Default parameters	Brute Force	Genetic Algorithm 1
Average error		1.9 / 3.9 / 4.7	1.8 / 2.4 / 4.5	1.8 / 3.7 / 4.7
Max error		4.7 / 7.4 / 8.8	4.2 / 5.1 / 8.3	4.4 / 7.3 / 8.6
Ratio of error	< 1mM	53 / 37 / 28 %	54 / 46 / 25 %	55 / 34 / 26 %
	< 3mM	79 / 58 / 51 %	80 / 71 / 53 %	80 / 58 / 52 %

A. Discussion of Results

The results almost fully confirm our expectations as the model training reached more than 20% improvement in the results. The improvement could be even higher with a longer training sample which was only one day in our current tests. We need more data logs for further tests.

Our results are not far from the best results published in the literature. Many other researchers used the Medtronic Guardian CGM system, which indicates that this is a state-of-art device to validate a blood glucose level prediction model. Likewise, in our validation, Stahl et al. [4] had the

same difficulties with the high peak values and they reached 1 mmol/l error in 95% of the cases with 2-hour-ahead prediction. We reached 1 mmol/l error in 46% of the cases with a 2-hour-ahead prediction during controlled tests. We can still improve this result by handling long-term basal insulins, such as Lantus. We experienced that our model can not simulate these long-term insulins properly. The other remarkable result is by Shanthi et al. [8], where the average error was 1.11 mmol/l for 60 minutes prediction, while Plis et al. [9] reached 1.99 mmol/l for 60 minutes. Our best result is 1.8 mmol/l for this period of time with the parameter identification in the controlled measurement.

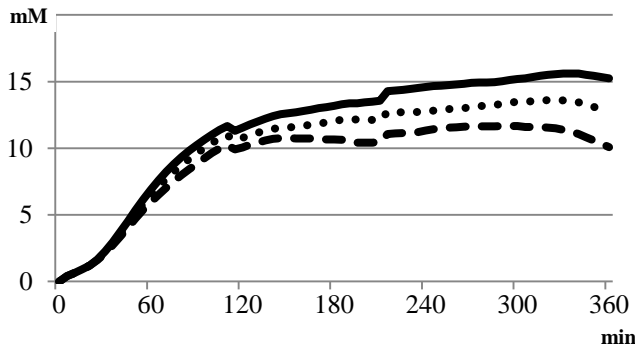


Figure 2. Average errors between measured and estimated values in time (solid line – default parameters, dotted line - GA 6 parameters, dashed line - BFA 6 parameters)

As it can be seen on Figure 2, the error is rapidly increasing during the first 2 hours, but the increase slows down between 2 and 6 hours. This shows that the long term

prediction is stable but the difference between the measured and the estimated values is still too large. The graph also shows that the improvements of the model training methods are significant only after the first hour. As we expected, the Brute Force Method gives the best result and the GA is between the BFA and the untrained results.

V. SOFTWARE

A software tool has been designed to support the validation process (Figure 3). The main idea was to provide a useful user interface, which helps us to run the calculations, collect, and process the information. All the data are stored in a relational database. To make the data access faster and consistent for each person participating in the research we chose the PostgreSQL open source database. The patients are organized into groups for the purpose of distinctness by medical experiments.

For the implementation of the graphical user interface (GUI) we chose the Qt cross-platform application framework and the C++ programming language. Exporting the results to PDF gives us the opportunity to share via e-mail or display on any other devices.

With the GUI, the user can select the proper episode of the patient, the start time, and the stop time. The tool lists all the meals, insulins, and measured blood glucose levels. The parameters of each algorithm can be modified before the calculation. After the calculation, the results are shown on graphs and tables. The algorithms also provide the optimized values of the parameters. All result are saved in the database for further analysis.

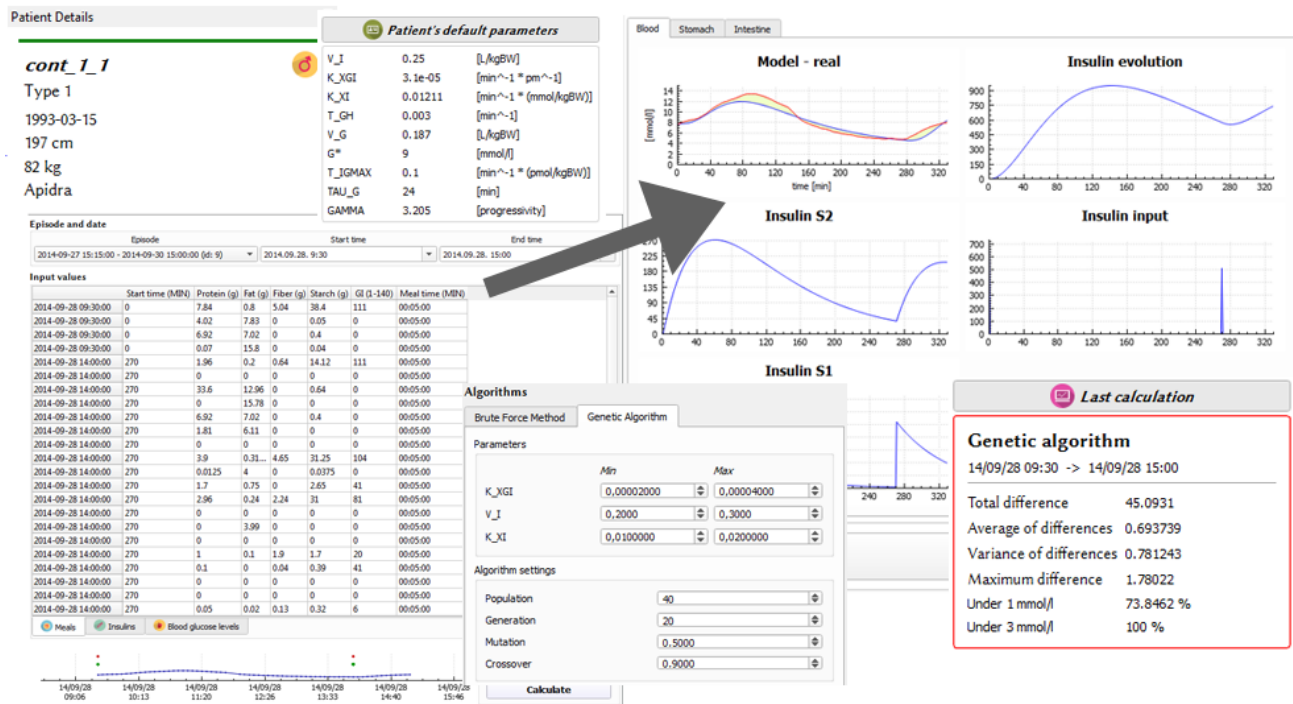


Figure 3. GUI of the software tool: input datas, output graphs and calculated results

VI. CONCLUSION AND FUTURE WORK

As for the difference between the controlled and all the data, we can state that a more precise logging is needed from the patients. To support this, we plan to create detailed manuals about the important events that should be precisely logged. A clinical study involving 20 diabetic patients will be made in the near future. Extending the 1 day model training period to at least 3 days should bring better results as well.

To solve the problems presented in section IV, future research is needed for:

- improving the currently used model training methods
- training the model with other parameter identification algorithms
- extending the model to support physical activity, stress, and weather changes.

The final aim is to decrease the average error under 1 mmol/l during the first hour and under 3 mmol/l during the first 4 hours. If the model proves reliable in clinical trials, it will be integrated into the Lavinia lifestyle mirror mobile application [24] developed at University of Pannonia [25].

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