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A Diabetes Self-Management Prototype in an AAL-Environment to Detect Remarkable Health States

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Abstract: Every year life span is increasing and simultaneously the proportion of people with one or more chronic diseases. This paper presents an implementation of a prototype with a decision tree to detect dangerous health conditions for Diabetes Type 1 and Diabetes Type 2. With the information we collect from Personal Health Devices and data from the Active-Assisted-Living environment, we are in the position to customize thresholds and to get individual results. With the help of a modified Glucose-Insulin Model (based on the minimal model of Stolwijk & Hardy) we predicted the future glucose concentration of the patient. We validated our model with an intention-to-treat pilot study including 8 subjects and obtained a significantly better ($p < 2.2^{-16}$) result than the original model.

Keywords. Decision Tree, Diabetes Mellitus, Glucose-Insulin Model, Stolwijk & Hardy model, AAL

1. Introduction

In the coming years the aging population in Europe will become a major challenge. In Austria the proportion of the older section (over 64 years) of the population grows every year by 0.25% (2012: 17%, 2020: 20%, 2060: 29%) [1]. In Europe 86% of deaths are caused by chronic diseases [2]. In center of focus is not only the individual health of the population, but are also many economic motives. If the potential of self-management (in a context of mobile Health) is fully exhausted by 2017, there is the possibility to save about €99 billion in healthcare costs in the EU (with an investment of €6.2 billion). Following the trend of self-managing health conditions, the World Health Organization (WHO) sees patient self-management as an essential component for chronic disease care [4]. Reasons are: early diagnosis and better treatment; patients care for their own health and have a healthier lifestyle; increased prevention; more effective and sustainable healthcare; health care professionals will be in the position to save 30% of their time spent on accessing and analyzing information [3].

The aim of this study was to implement and validate a routine to detect remarkable health states of patient with diabetes mellitus (DM). In the following chapters we will present the decision tree and the message types it use. In addition we describe the

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methods we used to modify the existing original glucose-insulin model and the results of the validation study.

There are two projects with a similar targets that is to empower patients with Active-Assisted-Living (AAL)-technology: EMPOWER[5] and MODULAAR[6].

2. Methods

In our overall study we implemented two additional checking routines (Hypertension and Heart Failure). In this paper we focus only on the glucose concentration routine.

2.1. Checking Routine

The routine generates four different message types *1) Alert; 2) Warning; 3) Information; 4) Activity* news and gets data from different health devices in the AAL environment, like in our case a glucose meter and temperature meter.

The routine uses a knowledge-based method, decision trees. We chose this method, because it is commonly used in medical sector and easy to understand for care staff and patients. The checking routine follows the example of Vukovic [7].

Glucose concentration Routine: We implemented the check-up of the glucose value, delivered by a glucose meter. Every time a physical health device (PHD) sends a new value, the implemented modified glucose-insulin model delivers a prediction of the future glucose values for the rest of the current day. The routine checks if any value in the prediction is above or below the thresholds, if so a message is generated.

2.2. Glucose-Insulin Model selection & modification

To create an alarm system for DM we *needed* to predict the future blood glucose concentration values. There are some well documented and commonly used models, but none of them use data from an AAL-Environment to improve their results. To our knowledge, no other glucose-insulin model has been altered with more than one modification. Based on the information from Knudson[8] we chose the minimal model of Stolwijk & Hardy[9] (Equation 1 and 2) as the basis for our six modifications*, which are:* 1) Oral one time glucose intake [10]; 2) one time i.v. bolus insulin [14]; 3) alcohol intake [11-13]); 4) fever/infections [15-16]; 5) exercise [17-22]; 6) mental stress [23] We *chose* these six, because of their well-documented influence on blood glucose concentration..

$$\frac{dG(t)}{dt} = \frac{Q_G - \lambda * G(t) - \nu * G(t) * I(t) - \mu * [G(t) - A]^+}{VD} \quad (1)$$

Q_G [mg/min] is the constant glucose inflow from the liver, the constant insulin independent glucose absorption λ [ml/min], ν [ml^2 / (mU * min)] is the constant insulin dependent glucose absorption and μ [mg/min] is the constant glucose clearance.

$$\frac{dI(t)}{dt} = \frac{-\alpha * I(t) + \beta * [G(t) - B]^+}{VD} \quad (2)$$

Table 1. Start parameter values

Parameter	Healthy Person	DM Type 1	DM Type 2
Q_G [mg/min]	140	140	140
λ [ml/min]	41.17	41.17	41.17
ν [ml² / (mU*min)]	2316.67	2316.67	463.33
μ [mg / min]	120	120	120
A [mg / ml]	2.5	2.5	2.5
B [mg / ml]	0.51	0.51	0.51
α [(ml*mU) / (mg*min)]	126.67	126.67	126.67
β [(ml*mU) / (mg*min)]	23.83	4.77	23.83

α [ml/min] and β [(mU * ml) / (mh * min)] in Equation 2 are constants for insulin absorption/production. The corresponding thresholds are *A* (glucose clearance) and *B* (insulin production).

In Table 1 we show the start parameter values according to Kumar [24] we used in the implementation of the model.

2.3. Model validation:

To validate our model we set up a study with 8 subjects (7 DM Type 1 and 1 DM Type 2 patients). The inclusion criteria *were*: 1) men and women between 25 and 99 years; 2) DM Type 1 or Type 2; 3) physically and mentally capable of doing this study. The exclusion criteria are: 1) other chronic diseases then DM Type 1 or Type 2; 2) pregnancy. We ask to record every 1) intake of food; 2) intake of alcohol; 3) intake of insulin; 4) change of basal insulin input rate by pump; 5) timeframes of moderate or dramatic stress; 6) change in health conditions; 7) exercise intensity for three days. The days *need not to be* batched. Additionally the subjects *had* to measure their blood glucose concentration at least 6 times a day and *completed* a questionnaire about demographic information and *we checked* the inclusion criteria. The questionnaire included the following questions: 1) Name; 2) PatientID (assigned by the study responsible); 3) birthday; 4) weight; 5) height; 6) sex; 7) chronic diseases; 8) drinking habits; 9) acute diseases; 10) insulin needed?; 11) using of insulin pump and 12) medication. *As we did*n*'t know* the patients *glucose and insulin concentration of* on *the first day at midnight, we set the start value to G(0) = 120 and I(0) = 1 (DM Type 1) / 10 (DM Type 2).*

Our null hypothesis is that the difference of the measured value and the *predicted* value of the modified model is greater or equal than the difference of the measured value and the *predicted* values of the original model of Stolwijk & Hardy. The alternative hypothesis is that *predicted* glucose concentration values have smaller variance to the measured values than the original model of Stolwijk & Hardy. We decide to take the absolute value of the difference between the measured values and the *predicted* values for the statistical analysis.

The study was following the rules of an intention-to-treat study [25]. We choose the one-side, depending t-test for paired samples with $\alpha = 0.05$ to test our hypothesis. The study protocol was approved by the Ethics Committee of the Medical University of Vienna (EK 1684/2016).

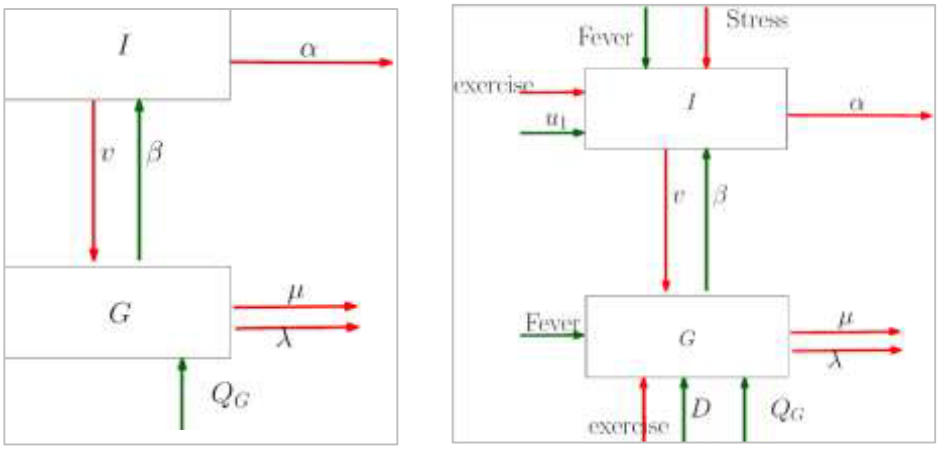

Figure 1. Original Model Stolwijk & Hardy (left) and modified model (right)

3. Results

3.1. Modified Glucose-Insulin Model

Figure 1 (left) shows the original minimal model by Stolwijk & Hardy [9]. In Figure 1 (right) you can see our modifications. The green arrows increase the concentrations in the compartment the red one will decrease them. Equation 3 and 4 show the new differential equations.

$$\frac{dG(t)}{dt} = G_e + \frac{Q_G*\left(1-C_g(t)\right)-\left(\lambda*G(t)-\nu*G(t)*I(t)-\mu*[G(t)-A]^+\right)*H(t)*S(t)+D(t)}{VD} \quad (3)$$

$$\frac{dI(t)}{dt} = -I_e(t) + C_i(t) + \frac{-\alpha*I(t)*H(t)+u_1(t)+\beta*[G(t)-B]^+}{VD} \quad (4)$$

D(t) describes the oral glucose intake of a meal.
$C_i(t)$ and $C_g(t)$ are the effects of alcohol on the glucose and insulin value.
H(t) is the reduced disappearance rate in case of an infection. In the implementation of the prototype we take 0.43.
S(t) is the factor to influence the glucose metabolism in case of mental stress. We decide to have two grades of stress level. Moderate stress S(t) = 1.17 and dramatic stress S(t) = 1.34.
$G_e(t)$ and $I_e(t)$ integrate the effect of exercise; $u_1(t)$ is the intake of insulin.

3.2. Parameter Prediction:

After a new glucose measurement is stored, we used a non-linear regression model to *predict* two parameters in our model: β and ν. We *chose* these two because they are the only two parameters which differ between *a healthy person and one that suffers of DM Type 1 or 2*. In our study we *predicted* β values between 0 and 28.847 and ν values between 0 and 2316.7 (lower bound was 0).

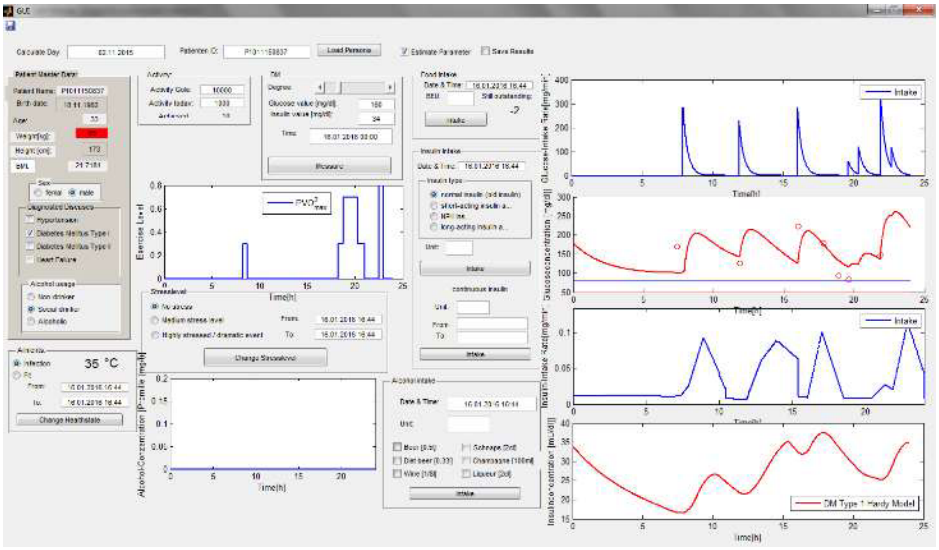

Figure 2. Matlab GUI Prototype

3.3. Prototype Implementation:

The main focus of the implemented prototype in Matlab R2012b was to give a clear overview of the input and output parameters of the modified model. This prototype *helped* to test and verify the model during the implementation process and study evaluation. In Figure 2 the GUI is depicted, *in which all* input parameters can be inserted.

3.4. Pilotstudy: Validation of the Glucose-Insulin Model:

As previously mentioned, we started a study to validate if the *predicted* glucose values of the modified model are closer to the measured values than the *predicted* values of the original model of Stolwijk & Hardy [9]. Our study participants did 221 glucose measurements with a mean value of 149.39 mg/dl ± 55.78 mg/dl. We decided to analyze the absolute distance between the measured values and the *predicted* ones, which lead to a mean range of 59.23 mg/dl ± 52.6 mg/dl for the modified model and 105.38 mg/dl ± 59.79 mg/dl.

As illustrated in Figure 3 the density of the predicted values of the modified model seems to match the density of the measured value much closer than the density of the original model. The variation of the absolute differences of both models is normally distributed, so we use the t-test to check our hypothesis: $p < 2.2\text{-}16$ $[-\infty, -38.0916]$. The modified model has a significantly smaller variance between the measured value and the predicted one.

4. Discussion

We have implemented a checking routine to show the user if he/she is in a dangerous health condition and we also indicated that our modified model is significantly more

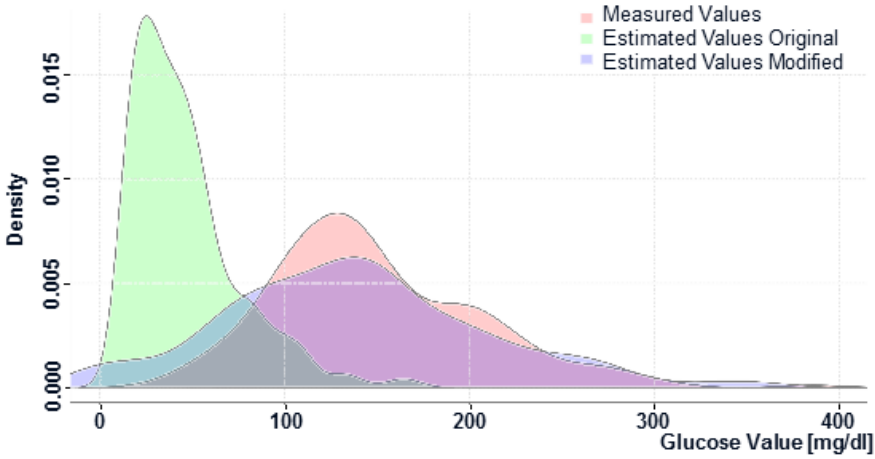

Figure 3. Density of the measured values and the predictions of both models in mg/dl

exact than he original model. However, there are some limitations to be taken into consideration:

4.1. The chosen simple Glucose-Insulin Model

Not all hormones which influence the glucose level are represented in the model.[9] Furthermore we use step functions in the model, though in nature no biological processes are like. A sigmoid function would be closer to the biologic reality. Another critical point is that insulin production is not an ongoing process, it is produced in squalls. [26]

4.2. Modifications of the Glucose-Insulin Model

In this model we don't distinguish between different types of sugar (e.q. fructose, sucrose), but according to Viljoen et al [27] there are *differences* in the absorption rate and elimination rate of alcohol. Additionally we choose two parameters to *predict*, but it would be better to *predict* all of them and use additional factors (e.g. glucose intake efficiency, insulin intake efficiency). Due to the fact that we don't have enough data to do that, the trial to *predict* all known parameters *ended* in some cases with unrealistic results.

There are a few ways to solve differential equations numerically. We choose one of the simplest, because the variation between the simple solution and the costly one (needs 175% more time) was only 61.5 mg/dl during one day (= 0.0427 mg/dl each minute). There is a permitted variation of 20% of any glucose meter [28], so we know that the collected data is impured by some variation as well. We therefore decided to accept the error produced by the numeric calculation of the differential equation.

4.3. Validation of the Glucose-Insulin Model

All values were measured from the patients themselves. Thus we rely on this data to operate the PHDs correctly and to note all relevant figures accurately. At the same time

the number of subjects is too small to make a comprehensive prediction about the significance of the model, but can give a precedent for new studies in this research area. Additionally, we had only one volunteer with DM Type 2. Unfortunately, we don't have the starting glucose and insulin values for the first day at midnight, so we had to set a fixed starting value.

It has to be mentioned that the influence of the i.v. bolus insulin on the glucose concentration is unnatural high in the original model. Most of our subjects use insulin or medication to lower their glucose concentration. This might be the answer, why the mean predicted glucose concentration is that low.

Nevertheless the parameter for the modifications are easy to monitor and the risk state detection is a helpful addition in an working AAL-Environment. Of course we try to eradicate some of this limitations during our project to improve the actual results even more.

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