PART III: COMPUTERIZED HEALTH BEHAVIOUR SUPPORT

In this part the possibilities of agent-based modelling and support are explored in the domain of health related behavior change. The scope of the models described in this part is quite broad: the models can be utilized both for chronic patients and for healthy individuals who want to change their health related behavior, to develop new healthy habits, to become aware of old habits or to adopt a healthy lifestyle. The models were developed at different levels of abstraction: both at an individual and at a group level across the agents clustering dimension; physiological, cognitive and behavioral across the process abstraction dimension; and at a local and global levels in time dimension. In Chapter 7 an intelligent support model for diabetic patients is described. The model gives advice about insulin intake based on the blood sugar level and daily activities and simulates the effect of advised insulin intake on the blood sugar level of an individual with diabetes type 2. This model is positioned at a local level across all three dimensions of the classification cube. Chapter 8 proposes a computational model of habit learning to support lifestyle change at an individual level. The model is located at an intermediate level of process abstraction dimension and at local levels of time and agents cluster dimension. In Chapter 9 a computational model of habit learning to support lifestyle change is extended with social influence. The model can be incorporated in a personal ambient intelligent agent that can enable lifestyle support. This model is located at intermediate levels of process abstraction and agent cluster dimensions and at a local level across time dimension. In Chapter 10 an intelligent model-based support system for therapy adherence and behavior change and its preliminary evaluation is described. The model described in Chapter 10 is situated at an intermediate level in process abstraction dimension and local levels in time and agent cluster dimensions.

Chapter 7

An Intelligent Support System for Diabetic Patients

This chapter appeared as:

Hoogendoorn, M., Klein, M. C. A. and Mogles, N.M. (2010). An Intelligent Support System for Diabetic Patients. In: *Fred, A., Filipe, J., Gamboa, H. (Eds.):Proceedings of the Third International Conference on Health Informatics, HEALTHINF'10*, INSTICC Press, 2010, pp. 98-105.

(Authors with comparable contributions)

An Intelligent Support System for Diabetic Patients

M. Hoogendoorn[1], M. C. A. Klein[1] and N. M. Mogles [1]

[1]VU University Amsterdam, Department of Artificial Intelligence
De Boelelaan 1081, 1081 HV Amsterdam
{mhoogen, mca.klein, nm.mogles}@few.vu.nl

Abstract. Diabetes Mellitus type I is a disease that forces patients to manage their blood glucose level manually, by balancing their activities, food intake and insulin dosages. There is a large experience with building computational models for blood glucose level in diabetic patients, which are primarily used to design the medication regime for a specific patient. In this paper, the design of an intelligent support application is presented that uses a standard model for blood glucose level to give patients real-time advice about insulin and food intake. The advice is based on measurements of blood glucose level, the electronic agenda of a patient and model-based predictions of the glucose level in the near future. A simulation of the application is presented that illustrates the feasibility of the system.

Keywords: diabetes, model-based reasoning, intelligent support

1 Introduction

Diabetes mellitus is a syndrome that is characterized by dysfunctional metabolism, resulting in too high blood sugar levels. According to the World Health Organization, the prevalence of diabetes for all age-groups worldwide is estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030 (Wild *et al*, 2000).

The glucose level in humans is regulated by a mechanism that is composed of several interacting systems, in which the hormone insulin is the very important, as it decreases the blood glucose level. There are two types of diabetic patients: in type 1 patients, the high blood glucose levels are caused by the loss of the insulin-producing cells in the pancreas, in type 2 patients the body developed a reduced sensitivity (or even resistance) to insulin.

Diabetes mellitus is currently a chronic disease, without a cure, and is treated by a combination of dietary guidelines, exercises and insulin supplementation. The main challenge for diabetes patients is to manually keep their blood glucose level within a safe range, by balancing both their glucose intake, their physical activities as their insulin dosages (note that type II patients are not always treated with insulin). This management is complicated and a burdensome task for diabetic patients. Specifically, the following reasons are mentioned (Wikipedia, 2009):

1. The glucose cycle is a system which is affected by two factors: entry of glucose into the bloodstream and also blood levels of insulin to control its transport out of the bloodstream;
2. As a system, it is sensitive to diet and exercise;
3. It is affected by the need for user anticipation due to the complicating effects of time delays between any activity and the respective impact on the glucose system;
4. Management is highly intrusive and compliance is an issue, since it relies upon user lifestyle change and (often) upon regular sampling and measuring of blood glucose levels, multiple times a day in many cases;
5. It changes as people grow and develop;
6. It is highly individual.

In this paper, we investigate the options for an intelligent support system that helps diabetic patients controlling their blood glucose, exploiting measurements via sensor devices, information about activity from electronic agenda's and model-based predictions of the blood glucose level. One of the features of such a system could be automated tuning of the model parameters to an individual patient. Together, such a system would ease the management of diabetes for patients in several aspects. The usage of a glucose-insulin model automates the assessment of the interaction of the different factors (complexity 1 & 2 in the list above), the prediction and usage of electronic agenda information automates part of the anticipation (number 3 in the list), while parameter tuning allows for personalization and adaptation over time (complexity 5 & 6).

In the next Section, we describe the main factors of blood glucose regulation process in the human body and a mathematical model that is often used for describing the glucose-insulin interaction. Section 3 sketches the main elements of an intelligent support system using the glucose model and sensor measurements. In Section 4 we show a number of simulations of patients with different activity patterns and the effect of an intelligent support system consisting of the components described in the section before. Finally, Section 5 concludes the paper.

2 Modeling blood glucose level

Mathematical or computational models of diabetes type I have been under development for several decades (see e.g. Bolie, 1961, Ackerman, 1965, Sorensen, 1985, Puckett, 1992, and Leaning and Boroujerdi, 1991). Models range from ordinary systems of differential equations to stochastic differential equations. Makroglou *et al* present a nice overview of the various types of models that exist. Within the ordinary systems of differential equations, the model used most frequently is the so-called *minimal* model which has been introduced by Bergman. The development of the model has been motivated by a desire to model the intravenous glucose tolerance test. Such models consist of many parameters that are very specific towards patients. As a result, parameter estimation techniques have been proposed that allow the tailoring of the models towards the patients. In (De Geatano and Arino) the results of one of such parameter estimation techniques are shown, namely a quasi-Newton minimization algorithm.
In this paper, the minimal model as introduced by Bergman *et al* (1979; Tololo *et al* 1980) is adopted. The model consists of the following three formulas:

$$\mathrm{d}G(t)/\mathrm{d}t = -[p_1 + X(t)]G(t) + p_1 G_b \qquad (1a)$$
$$= -X(t)G(t) + p_1[G_b - G(t)] \qquad (1b)$$

$$\mathrm{d}X(t)/\mathrm{d}t = -p_2 X(t) + p_3[I(t) - I_b] \qquad (2)$$

$$\mathrm{d}I(t)/\mathrm{d}t = p_4[G(t) - p_5]^+ \, \mathrm{t} - p_6[I(t) - I_b] \qquad (3)$$

In this formula, $G(t)$ is the blood glucose concentration, $I(t)$ is the blood insulin concentration, and $X(t)$ is related to the interstitial insulin level, i.e. the insulin that is at a location where it can actually effect the glucose uptake by cells. Furthermore,

- G_b is the subject's baseline glucose level;
- I_b is the subject's baseline insulin level;
- p_1 is the glucose “mass action” rate constant, i.e. the insulin-independent rate constant of tissue glucose uptake;
- p_2 is the rate constant expressing the spontaneous decrease of tissue glucose uptake ability;
- p_3 is the insulin-dependent increase in tissue glucose uptake ability;
- p_4 is the rate of pancreatic release of insulin after glucose intake;
- p_5 is the pancreatic “target” blood sugar level;
- p_6 is the decay rate constant for insulin in plasma;

For patients with diabetes type 1, we assume that the pancreas does not produce any insulin anymore. In the model, the effect is that parameters p_4 and I_b are zero. Consequently, the insulin level is determined only by the artificial intake of insulin and the decay, with $I_s(t)$*denoting* the artificial insulin supply at certain time points:

$$\mathrm{d}I(t)/\mathrm{d}t = -\, p_6[I(t)] + I_s(t) \qquad (4)$$

The minimal model does not take the effect of physical effort into account. The effect of physical effort on the insulin and the blood glucose balance is twofold:

- it increases the insulin use by cells;
- it lowers the glucose concentration during and after the exercise (Goodyear and Kahn, 1998).

Especially the fact that the glucose concentration is also lowered *after* the exercise (up to 24 hours) is an important factor to take into account. According to (Derouich and Boutayeb, 2002), the minimal model extended with the effect of exercises can be described by the following formulas:

$$\mathrm{d}G(t)/\mathrm{d}t = -\,[1 + q_2]\, X(t)G(t) + [p_1 + q_1][G_b - G(t)] \quad (5)$$

$$\mathrm{d}X(t)/\mathrm{d}t = -\, p_2X(t) + [p_3 + q_3][I(t) - I_b] \qquad (6)$$

In these formulae, the q-parameters define the effect of physical activity. They are defined as follows:

- q_1: the effect of the physical exercise in accelerating the utilization of glucose by muscles and the liver.
- q_2: the effect of the physical exercise in increasing the muscular and liver sensibility to the action of the insulin.
- q_3: the effect of the physical exercise in increasing the utilization of the insulin.

The q_2 variable is also larger then 0 for some time after the exercise.

3 Intelligent Support

Currently, diabetes patients design a schema for insulin intake in consultation with their medical practitioner. This schema is based on a registration of regular blood glucose measurements. Patients will also use their common sense knowledge about the effect of their activities on their blood glucose level: for example, if a large meal is consumed, the person will take a somewhat higher dose of insulin, or if sporting activities are planned, some additional food (especially) carbohydrates will be taken. In addition to this, patients will do regular blood glucose measurements to verify whether it is still within safe bounds, and possibly to correct it.

Figure 1. Electronic blood glucose meter.

The envisaged intelligent support system will give advice to a patient on when to take which amount of insulin or a meal. This advice is based on a prediction of the blood glucose level using the most recent measurement and the activities listed in the electronic agenda. The listed activities influence the blood glucose level, but also determine the time points when insulin or a meal can be taken. For example, in the middle of a sporting activity of while working, it is not easily possible to take a meal or insulin. The system could be implemented as an advanced mobile phone or PDA application. Blood glucose measurements will ideally be transferred from the electronic device (see Figure 1) via a wireless technology such as Bluetooth, but could also be manually typed in into the application.

For the prediction of the glucose level, the model as explained in the previous section is used. The parameters in the model should be fitted to the personal characteristics of the patient. For this fitting, there are quite a number of approaches (De Geatano and Arino, 2000). In this paper, we assume that the parameter fitting has been implemented using one of the described techniques. Our intelligent support system will use the model with the fitted parameters and dynamically determine the amount of insulin to be taken.

The system internally uses a list of activities and associated values for the q parameters. Each type of activity can have different parameters. For example, walking could have different parameters for the utilization of glucose and insulin than intense sporting. The activities are read from the agenda, and from the latest time point of measurement, the current glucose level is calculated based on the activities that are undertaken since the last measurement. In addition, the upcoming activities are used to predict the blood glucose level at the end of the *next activity* that still has to be started. For example, when a person is currently working and the next activity will be cycling, the glucose level at the end of the cycling activity is measured. In case this measurement is too high, advice is given to take insulin at the end of the *current* activity. In case this measurement is too low, advice is given to take some food at the end of the *current activity*. The amount of insulin or food is dynamically determined by simulation within the support system. At the end of the current activity, the patient will get a message, for example via his mobile phone application, to take a specific amount of insulin or food before the next activity.

4 Simulation Experiments

The model and prediction rules that are used by the system have been implemented in Matlab. A number of simulation experiments have been run in this environment. In these experiments, the activities of a person during two consecutive days are simulated. Table 1 gives an overview of the activities and the time points. Note that the simulation time uses units of 15 minutes.

For the parameters, values were used that are found in the literature as realistic values for a specific person. Specifically, we used the parameters of subject 2 in (Gaetano and Arino, 2000): $p_0 = 100$, $p_1 = 0.1$, $p_2 = 0.2196$, $p_3 = 0.0064$, $p_4 = 0$, $p_5 = 23$, $p_6 = 0.096$, $p_7 = 0.5$, $I_b = 0$, $G_b = 120$. Note that p_4 and I_b are 0 because we consider a diabetic patient. For the desired minimum and maximum glucose levels, we use 80 and 120 mg/dL (Erzen *et al*, 2000).

Table 1. List of activities during two days.

Activity	Clock time	Time points in simulation	
Sleeping till 7am	0:00	0	96
Breakfast	7:00	28	124
Cycling / driving	7:30	30	126
Office work	8:15	33	129
Coffee	10:15	41	137
Office work	10:30	42	138
Lunch	12:30	50	146
Office work	13:00	52	148
Tea	16:00	64	160
Office work	16:15	65	161
Cycling / driving	17:00	68	164
Diner	17:45	71	167
Relaxing	18:30	74	170
Intense sporting / no sporting	19:30	78	174
Relaxing	20:30	82	178
Sleeping till 0:00	22:30	90	186
Sleeping till 7am	0:00	96	192

4.1 Blood glucose level without insulin intake

The first simulation shows the blood glucose level for a person that does not produce any insulin anymore. At the start of the simulation, there is still a small amount of insulin available (0.5 μU/ml), however, this dissolve in a few hours. It can be seen that the blood glucose level will be almost always too high (see Figure 2).

4.2 Regular insulin intake with and without physical activities

In the second set of simulations the glucose level of a patient that is treated with a schema of regular insulin intake doses. We assume in the simulation that insulin is taken just before every meal, effectively three times per day. The second assumption is that a patient takes a lower dose of insulin if physical activities are undertaken during the day. We did this simulation for two different scenarios: one with physical activities, in which the person uses a bicycle to commute and does sporting in the evening, and one in which the person drives to his work by car and does no sporting. For the effect of physical activities on the blood glucose balance, we used a q_2 value of 0.25 for cycling and 0.5 for intense sporting. The effect of the duration of the q_2 effect was set to 24 hours. The parameters q_1 and q_3 were both set to 0.25; no empirical values were available. The effect on the blood glucose level and the insulin is depicted in Figure 3 and 4.

It can be seen in Figure 4 that the patient takes a smaller amount of insulin on a regular basis using his common sense to keep the blood glucose within safe boundaries in the scenario in which physical activities are undertaken.

4.3 Prediction of maximum and minimum glucose levels

To give a person intelligent support about his insulin intake, we have to predict the effect of the activities on the *future* blood glucose level. We do this by running a simulation of the future values of the blood glucose level during the current and next activity at every time point *within* the simulation of the scenarios. For this, we determine the end of the next activity, take the planned activities into account, and simulate the blood glucose level till the end of the next activity, assuming that no insulin will be taken. Then, the maximum and minimum levels of the blood glucose during that period are determined. Figure 5 illustrates how this would look for the scenario in which no insulin is taken (i.e. the scenario depicted in Figure 2; the jigsaw pattern is a side effect of using a small time step in the simulation.)

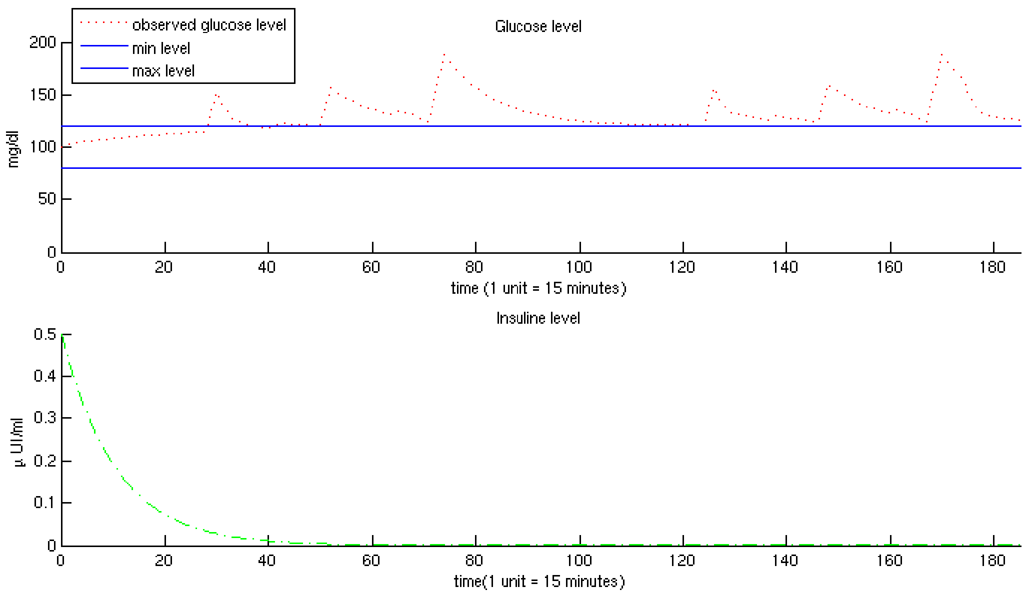

Figure 2. Blood glucose level of a diabetic patient without insulin intake.

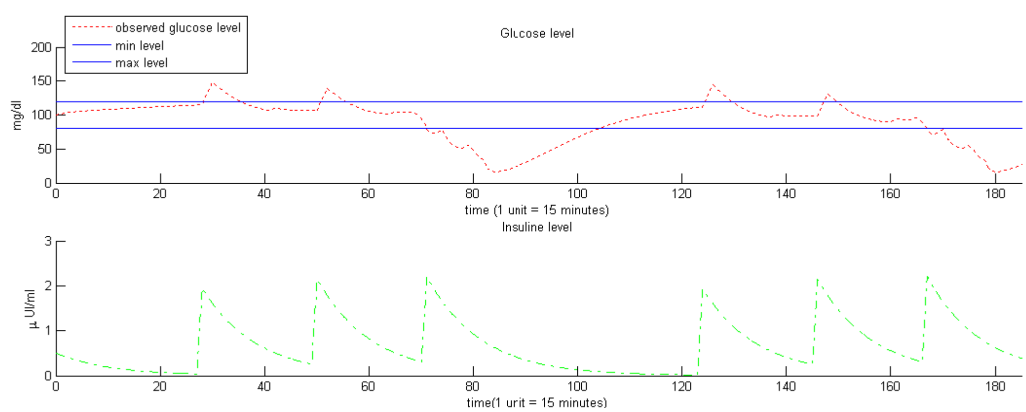

Figure 3. Simulation of a diabetic patient that takes regular insulin dose *with physical activities.*

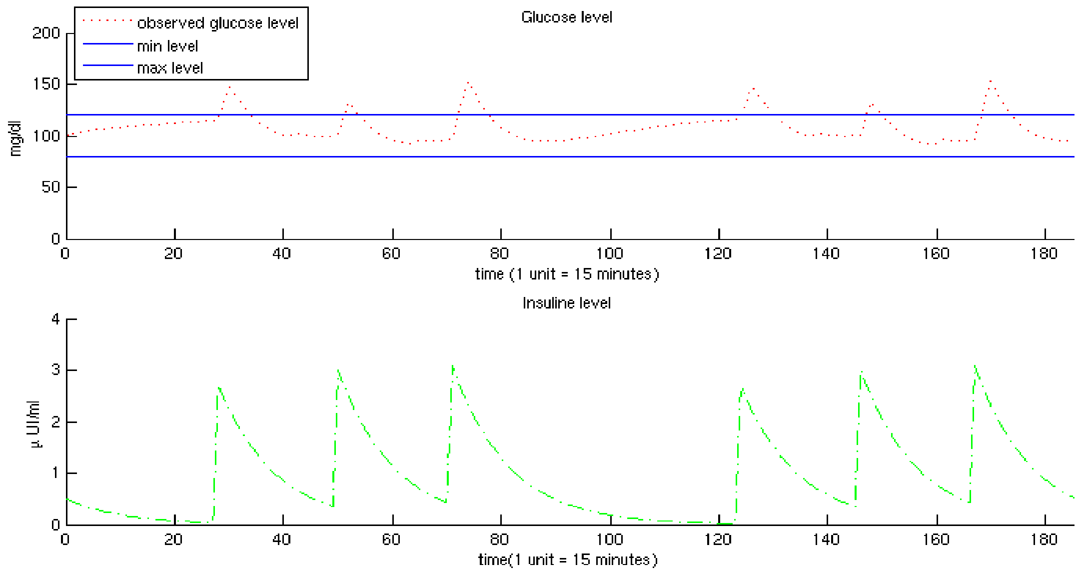

Figure 4. Simulation of a diabetic patient that takes regular insulin dose *without physical activities*.

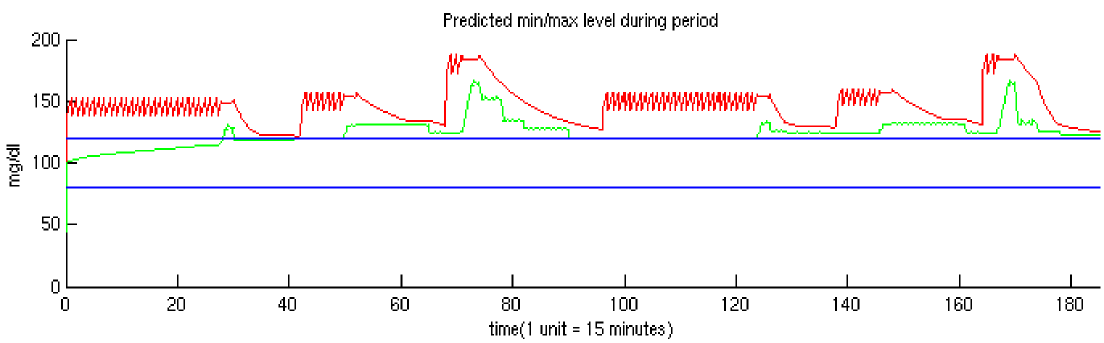

Figure 5. The predicted maximum and minimum blood glucose level during the current and next activity.

When it is predicted that the maximum glucose level will become too high (in this case > 120) till the end of the next activity, the system will run another simulation to predict the effect of taking a standard insulin dose at the end of the current activity. When it is predicted that the minimum glucose level will become too low (in this case < 80) before the end of the next activity, the system will run another simulation to predict the effect of taking a standard meal(e.g. a cup of coffee, a chocolate bar) at the end of the current activity. Based on the size of the effect, the optimal dose is determined. This is done by comparing the required effect and the achieved effect with the standard dose. For example, if a standard dose of insulin reduces the excess of the predicted level over the maximum level by 30%, the advised dose is 100/30 = 3.33 times the standard dose.

4.4 Using the intelligent support system for insulin and food intake

We also ran a number of simulations of scenarios in which patients actually follow the advice of the intelligent support system. In these scenarios, the advised dose of insulin is actually taken, and the effect of this insulin is taken into account in the next predictions. We show two scenarios: the first one is the one without physical activities (Figure 6), the second one with physical activities (Figure 7).

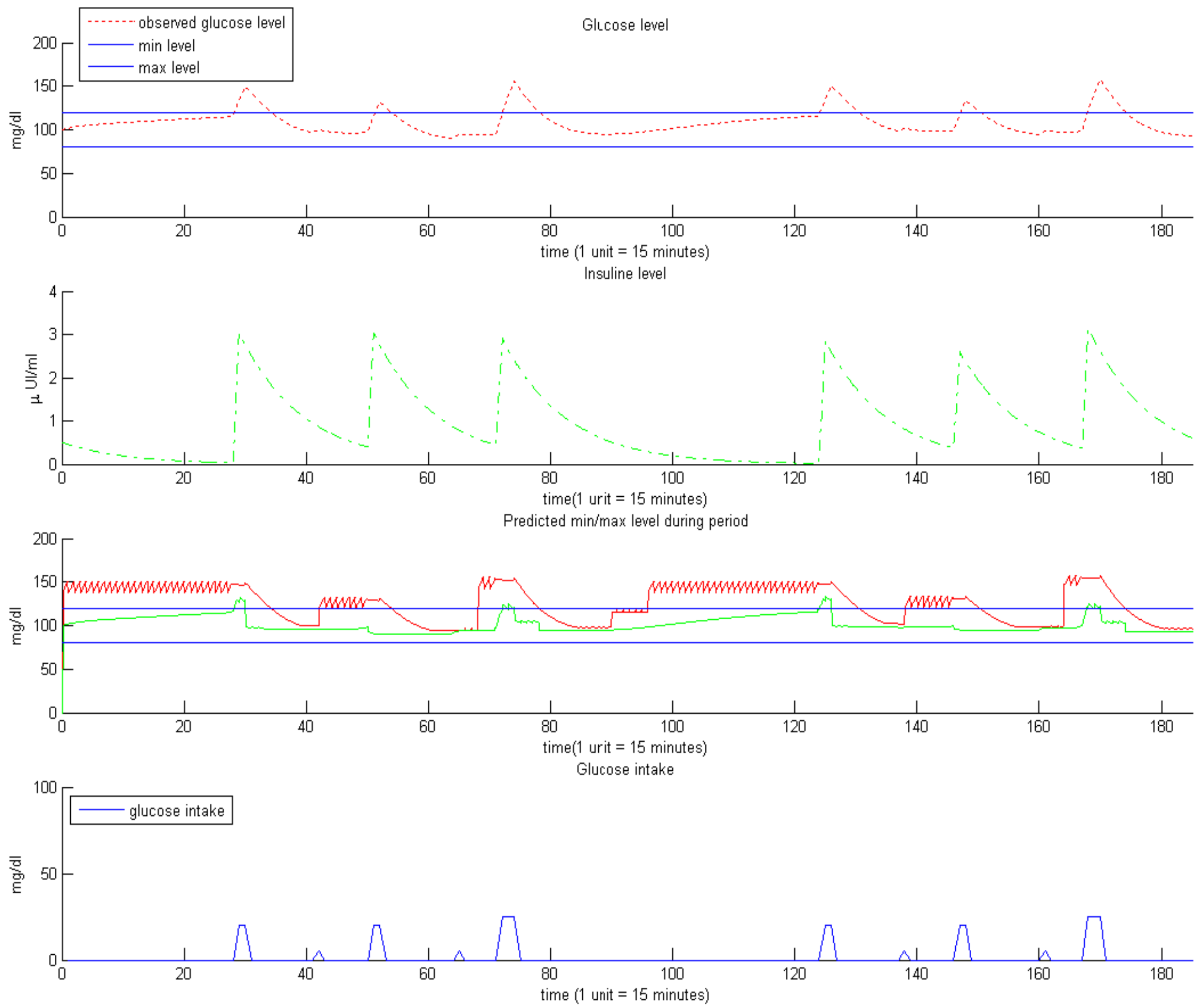

Figure 6. Simulation of a patient using the intelligent support system *without physical activities.*

The figures show that the system is able to adapt automatically to the activities of the person as registered in his electronic agenda. In the scenario without physical activities (Figure 6) the person gets advice to take insulin three times per day with a dose that corresponds to an insulin level increase of around 3 µU/ml in the blood. No advice about additional meals is given: it can be seen in Figure 6 that the glucose intake is standard and

corresponds to 5 time regular meals during the day, such as breakfast, coffee , lunch, tea and dinner.
In the second scenario (see Figure 7), the advice is to take insulin three times per day and five additional meals during the first day and three times per day insulin and one time an additional meal during the second day. During the first day of the second scenario the glucose intake occurs ten times a day instead of standard five and six times during the second day.
In both scenarios, the blood glucose level is most of the time below the advised maximum level and above the advised minimum level. Moreover, the advice is always given at appropriate times, i.e. never in the middle of an activity or during the night.

5 Discussion

In this paper, the working of an intelligent support system for diabetic patients is presented. The system is based on the existing technologies like mobile phones with electronic agenda's, electronic blood glucose meters, and mathematical models of the blood/insulin balance. Keeping the blood glucose level within the safe boundaries by balancing insulin dosages, glucose intake and physical activities is a complicated task for diabetes patients. The advantage of this system is that it adapts automatically to the personal schedule of a patient and gives concrete advice about insulin and food intake at appropriate time points if it predicts that the blood glucose level of the patient will rise above the higher boundary or drop below the lower boundary at the end of the next activity. The simulation results demonstrated that in the scenario with the patient's physical activities the intelligent support system helps better to maintain an appropriate blood glucose level in comparison with the regular insulin prescription.
Thus, the system could possible release a bit of the burden of diabetic patients as it can predict the effect of the upcoming activities more precisely than humans. Moreover, the effective blood glucose level management may minimize the progression of the disease and reduce the risk of later complications that accompany this chronic disease (Deutsch, 1994).

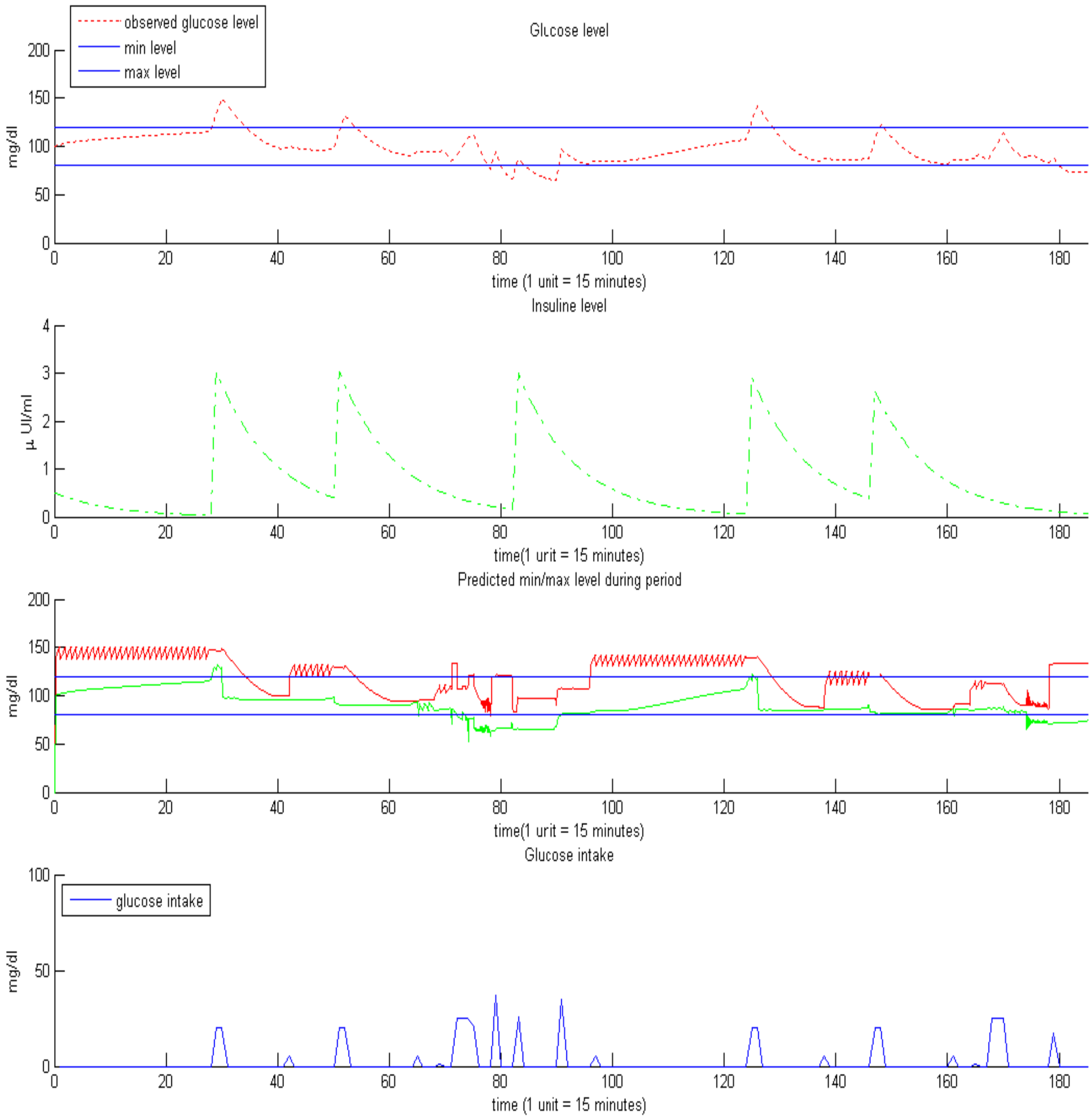

Figure 7. Simulation of a patient using the ambient support system *with physical activities.*

There are a number of extensions of this system imaginable. First of all, one could think of using continuous, non-invasive blood glucose measuring techniques. At the moment, those are not yet available, but it is expected that these become available in the near future. Second, more specific rules for restrictions on the advice can be implemented, for example the minimum of maximum dose, the minimal time between insulin doses, the maximum doses per day, etc. These extensions could make the system even more realistic and more effective for patients.

References

Ackerman, E., Gatewood, L. C., Rosevear, J. W. and Molnar, G. D., 1965. Model studies of blood-glucose regulation. *Bulletin of Mathematical Biophysics* 27:21-37.

Bergman, R. N., Ider, Y. Z., Bowden, C. R. and Cobelli, C., 1979. Quantitative estimation of insulin sensitivity. *American Journal of Physiology* 236: E667-E677.

Bolie, V. W., 1961. Coefficients of normal blood glucose regulation. *Journal of Applied Physiology* 16:783-788.

Derouich, M., Boutayeb, A., 2002. The effect of physical exercise on the dynamics of glucose and insulin. *Journal of Biomechanics* 35(7): 911-917.

Deutsch, T., Lehmann, E. D., Carson, E.R., Roudsari, A.V., Hopkins, K.D., Sönksen, P.H., 1994. Time series analysis and control of blood glucose levels in diabetic patients.*Computer Methods and Programs in Biomedicine* 41:167–182.

Erzen, F.C., Birol, G., Cinar, A., 2000. "Simulation Studies on the Dynamics of Diabetes Mellitus," bibe, pp.231, *IEEE International Symposium on Bio-Informatics and Biomedical Engineering (BIBE'00).*

De Gaetano, A. and Arino, O., 2000.Mathematical modelling of the intravenous glucose tolerance test, *Journal of Mathematical Biology* 40: 136-168.

Goodyear, L.J., Kahn, B.B., 1998. Exercise, glucose transport, and insulin sensitivity, *Annual Review of Medicine* 49: 235-261.

Leaning, M.S. and Boroujerdi, M.A., 1991. A system for compartmental modelling and simulation. *Computer Methods and Programs in Biomedicine* 35:71–92.

Puckett, W.R., 1992. Dynamic modelling of diabetes mellitus. *PhD Thesis, University of Wisconsin - Madison*.

Sorensen, J.T., 1985. Physiologic model of glucose metabolism in men and its use to design and asses improved insulin therapies for diabetes. *PhD Thesis, MIT*.

Tololo, G., Bergman, R. N., Finegood, D. T., Bowden, C. R. and Cobelli, C., 1980. Quantitative estimation of beta cell sensitivity to glucose in the intact organism: a minimal model of insulin kinetics in the dog. *Diabetes* 29: 979-990.

Wild, S., Roglic, G., Green, A., Sicree, R., King, H., 2004. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 27 (5): 1047–53.

Wikipedia, 2009. Diabetes management, section Complexities relating to management, http://en.wikipedia.org/wiki/Diabetes_management, retrieved at June 8, 2009.

Chapter 8

A Computational Model of Habit Learning to Enable Ambient Support for Lifestyle Change

This chapter appeared as:

Klein, M.C.A, Mogles, N.M., Treur, J. and Wissen, A. van. (2011). A Computational Model of Habit Learning to Enable Ambient Support for Lifestyle Change. In: *K.G. Mehrota et al. (Ed.)*, *Proceedings of the 24th International Conference on Industrial, Engineering and Other Applications of Applied Intelligent Systems*, Part II Vol. 6704. Lecture Notes in Computer Science, Springer Verlag, pp. 130-142.

(Authors with comparable contributions)