Glucose Level Prediction Using Artificial Neural Networks

EUGEN IANCU*, IONELA IANCU**, DAN ISTRATE***, MARIA MOȚĂ****
*Department of Automation, University of Craiova
Decebal Street, no. 107, 200440 Craiova
** Department of Physiology, Medical Informatics and Biostatistics
****Department of Diabetes and Nutrition Diseases
University of Medicine and Pharmacy of Craiova
Petru Rares Street, no. 4, 200349 Craiova
ROMANIA
***ESIGETEL – Ecole Supérieure d’Ingénieurs en Informatique et Génie des Télécommunications
Rue du Port de Valvins, 1, 77210 Avon-Fontainebleau
FRANCE
dan.istrate@esigetel.fr http://www.esigetel.fr

Abstract: - The advanced treatment of the type I diabetes mellitus through closed-loop systems, such as artificial pancreas is one of today’s greatest challenges. In this work the authors have tried to develop a predictive method which can be incorporated in an optimal system for blood glucose-insulin regulation. Using the neural network approach it is possible to compose a prediction model, very useful to control an insulin pump. Also, the artificial neural networks can be used to test and validate the medical decisions. The results of this study can be applied also, to other physiological systems, as it offers important data for the medical practice and it contributes to introduce the computer assisted diagnosis like a current medical method.

Key-Words: - diabetes mellitus, continuous glucose monitoring, neural network, modeling and simulation, blood glucose control.

1 Introduction

The aim of this paper is to develop a predictive neural network for blood glucose artificial control system. Predictive control is different from a closed loop feedback control where the desired operating point is compared with an actual blood glucose concentration point and the difference is fed back to the system. Predictive control problems are defined in their time domain, and their solution requires designing the course (future) of action so as to optimize a performance index [1], [2]. Therefore the predictive control allows us to make future decisions. Using the predictive control theory we can minimize deviations of blood glucose from normal levels, while penalizing the use of large amounts of infused insulin for safety.

The current treatment methods for insulin-dependent diabetes include subcutaneous insulin injection or continuous infusion of insulin via an insulin pump. The former treatment requires patients to inject insulin four to five times a day. The amount of insulin injected is usually determined by a glucose measurement, an approximation of the glucose content of the upcoming meal and estimated insulin release kinetics [3], [4].

The insulin infusion pump allows a constant and predictable delivery rate of insulin into a subcutaneous site. The efficiency of the predictive control system is to keep the blood glucose levels as close to normal as possible. This behavior is essential for preventing diabetes related complications. Ideally this level is between 60 and 120 mg/dl before meals and less than 180 mg/dl two hours after starting a meal.

Fig. 1. Model predictive control scheme.
All model predictive control (MPC) systems rely on the idea of generating values for process inputs as solutions of an on-line (real-time) optimization problem. That problem is constructed on the basis of a process model and a predictive algorithm. Figure 1 shows the structure of a typical MPC system.

2 Control of Blood Glucose Levels
The use of bolus subcutaneous injections of insulin for the control of blood glucose concentration in a diabetic patient is a normal clinical practice. Better physiological response should be obtained if the glucose level is monitored regularly and insulin delivered in a regime more closely resembling to the normal release mechanism. In simple terms, the B-cell delivers insulin into the blood stream at two rates:

- A continuous, slow basal rate, which controls glucose output from the liver;
- Mealtime bursts of insulin for the intestinal absorption glucose.

With the advent of continuous blood glucose monitoring and frequent sampling profiles it has become apparent that in most insulin-dependent diabetic patients it is difficult to sustain near normal blood glucose concentrations.

Therapy with insulin pump is recommended worldwide as the most effective and physiological method of treatment in diabetes mellitus type I (insulin-dependent). Some authors consider that the closed-loop system, (artificial pancreas) is the best solution [5]. An extra-corporeal blood glucose sensor is coupled to a programmable logic controller - PLC, which controls the rate of infusion of insulin into a subcutaneous site, so as to maintain normoglycaemia. Although very successful in maintaining normoglycaemia in diabetic patients for up a few days, it has major disadvantages for long-term use. Prolonged infusions carry the risk of thrombosis and infection.

In our study, an extra-corporeal sensor measures the blood glucose level. It is coupled to a logical unit for the management of decisions and to an artificial neural network (Fig. 2). Neural network, based on the measured values of blood glucose, has the task to predict the next value. Unit management of decisions includes a mathematical model of the patient. It receives input from two sizes: a signal representing measured values of blood glucose (from the sensor) and a signal from the neural network that represents the anticipated values. Processing of these signals, the decision management unit takes the following actions:

- Anticipates for the next period, the evolution of blood glucose level.
- Using the patient’s prediction model estimates the blood insulin concentration and calculates the necessary in insulin for the next step.
- Controls the rate of infusion of insulin into a subcutaneous site.

3 Neural Network Architecture
From a system point of view, the feed-forward network is only a static mapping between inputs and outputs [6]. The simplest approach in representing a non-linear dynamic system is to use a combination of feed-forward networks with some time delay units:

$$\hat{y}(k) = F[W, y(k-1),..., y(k-m), u(k),..., u(k-n)]$$

(1)

where $u(k)$ is the input and $y(k)$ is the output of the real system, $F(.)$ represents a non-linear function, $W$ is the weight matrix and $\hat{y}(k)$ is the estimated value of output. We have implemented a predictive algorithm by using a feedforward neural network to approximate the function $F$ (NARX model) [7]. A diagram of the resulting network is shown in figure 3, where a two-layer feedforward network is used for the approximation. Network receives five consecutive blood glucose values and predicts the expected value in step six.

![Fig. 2. The structure of the predictive system for blood glucose control](image)
4 Experimental Results

For this study we have selected 22 adult subjects (12 female and 10 male), patients with insulin dependent mellitus diabetes and 8 healthy humans. Sixteen patients underwent treatment with rapid and semi-lent types of insulin, at different times of the day, according to the classic method of treatment and clinically supervised. Patients maintain a satisfactory or poorly control of the blood glucose concentration for a long period of time. Six patients have received a proper dosage of insulin through a new device called insulin pump. This offers a continuous basal rate of insulin and facilitates the administration of bolus insulin related to meals, exercise or other particular states. These patients maintain a very good control over the blood glucose concentration for a long period of time. The blood glucose was recorded for each patient at five minute intervals, continuously for three days, using the Real-Time Guardian Continuous Glucose Monitoring System (CGMS) [8] in unrestrained conditions. Each patient had a normal life, with usual meals and activities at work and at home. The continuous blood glucose records represent for this study time-series of the blood glucose concentration. The following figures present the blood glucose evolution for 24 hours. For exemplification we choose the following individual cases:

- One patient (P1) with insulin dependent diabetes (type I) under intermittent treatment with insulin injections. The CGMS displays high variability of the glucose values as an expression of an insufficient control of diabetes (Fig. 4).

- One patient (P2) with insulin dependent diabetes under insulin treatment administrated by insulin pump. The CGMS displays a less variability of glucose values, expression for an improved control of diabetes (Fig. 5).

- One healthy subject (P3) with normal food administration and activity. The CGMS displays a low variability of the glucose values, expression of an efficient blood glucose control (Fig. 6).

![Fig. 4. Time evolution of the glucose concentration for the P1 patient. (INS–insulin treatment, M–meal)](image)

![Fig. 5. Time evolution of the glucose concentration for the P2 patient. (INS–insulin treatment, M–meal)](image)

![Fig. 6. Time evolution of the glucose concentration for the healthy subject (P3). (M – meal)](image)
The output of the network is an estimate of the blood glucose concentration. The output is fed back to the input of the feedforward neural network as part of the standard NARX architecture [7]. Because the true output is available during the training of the network, we have created a series-parallel architecture, in which the true output is used instead of feeding back the estimated output. This has two advantages. The first is that the input to the feedforward network is more accurate. The second is that the resulting network has a purely feedforward architecture, and static backpropagation can be used for training [7].

The network was trained for each patient separately (treatment with insulin injection or insulin pump) with the records provided by the CGMS Guardian type for 24 hours. Network behavior was tested using a different set of recordings, during 24 hours, taken from the same patients. Results are shown in the figures below.

![Fig. 7. Time evolution of the glucose concentration for a patient (P1) under treatment with intermittent insulin injections.](image1)

![Fig. 8. Time evolution of the estimated glucose concentration for the patient P1.](image2)

![Fig. 9. Time evolution of the prediction error calculated as a difference between estimated and measured glucose concentration for the patient P1.](image3)

![Fig. 10. Time evolution of the glucose concentration for the P2 patient (with insulin pump).](image4)

![Fig. 11. Time evolution of the estimated glucose concentration for the patient P2.](image5)
Fig. 12. Time evolution of the prediction error calculated as a difference between estimated and measured glucose concentration for the patient P2.

Fig. 13. Time evolution of the glucose concentration for the P3 subject (healthy subject).

Fig. 14. Time evolution of the estimated glucose concentration for the patient P3 (healthy subject).

Fig. 15. Time evolution of the prediction error calculated as a difference between estimated and measured glucose concentration for the patient P3.

5 Conclusion

A nonlinear auto-regressive neural network with exogenous inputs (NARX) was used to estimate the blood glucose concentration. The explicit NARX model obtained from the off-line identification procedure was then used to predict the effects of future control actions. The procedure enables the construction of a network from the experimental data, and consequently, allows the designing of a controller using multiple-step-ahead predictions of the blood glucose.

To predict future values of the glycaemia, we used a neural network in two layers. The first layer contains 10 neurons and uses a transfer function of the type \textit{tansig}. The 2nd layer contains a single neuron and has a transfer function of the type \textit{pureline}.

More exactly, the network uses five previous measurements of blood glucose values (which corresponds to a "history" of the past 25 minutes) and anticipates the level still to come. In this way the control system is ahead by 5 minutes in order to synthesise the insulin pump command.

Acknowledgments

This paper is part of the project \textit{The development of automated systems for blood-glucose control at insulin-dependent patients. The implementation of evolved algorithms for computer assisted monitoring and diagnosis}, at the University of Medicine and Pharmacy of Craiova and was supported by National University Research Council, Romania.
References:


[7] * * * Neural Network, MathWorks Tutorial, 1999.