CONTROL SYSTEM FOR INSULIN PUMPS IN THE MELLITUS DIABETES TREATMENTS

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Abstract: 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 of the pancreas. The pump of insulin represents the solution of the physiological request. In this work, different structure for control of the pump with maintained of blood-glucose level are analysed.

Key words: blood glucose control, insulin pump, modeling and simulation, mellitus diabetes.

1. INTRODUCTION

The mellitus diabetes is a chronic disease that develops a great risk of progression of diabetes complications: diabetes coma, retinopathy, nephropathy, neuropathy, liver damage, blindness, etc.
The treatment must be permanent and rigorous, and need multiple pricks to monitor blood glucose levels or to inject insulin. From 1980, the insulin pumps offer a new method for insulin administration.
The insulin pump is a small battery-operated device, size of a pager or cell-phone, that can be wear to the belt or pocket.

The pump reservoir contains the proper recommended insulin and delivers it to the body through a flexible plastic tube called catheter. With the aid of a small needle the catheter is inserted through the skin into the fatty tissue and is taped in place.
Pump continuously send micro-drops of insulin, every minute, 24 hours/day, according to a programmed plan unique to each patient. Also, pump delivery insulin for different moments of the day or situation: walking, physical exercise, sleep, mealtime, or in stress conditions.

So, insulin pump assures:

- Basal rate of insulin.
- Bolus doses to correct or supplement the necessary insulin for the body.

The pump can be linked to a glucose meter allowing transfer of the data from the glucose sensor to the pump to help analyse and choose doses that will be provided. An independent micro controller checks that each tenth of unit delivery of insulin does not exceed programmed settings.

The insulin pump is an exterior body device that works autonomous for 3 days. The administration of the insulin in bolus is realised by the diabetes patients that calculated mentally the amount of insulin needed in accordance with their individual experience and the medical recommendations. So, this method is not complete physiological, because it can result dosing inaccuracies that lead to less than optimal blood glucose control.
The artificial pancreas is an implantable insulin pump or a watch-like pump, that work autonomous for 3 months and contains: the sensor for glucose monitoring, the reservoir and the pump for insulin and predictive algorithms for blood insulin-glucose levels control.

Most of the algorithm are linear or simplified to approximate the function of the pancreas or others systems of the body. So, this algorithm approximate the level of insulin for reduce the peak of the glucose level. Other algorithm analyse data from past events to forecast future insulin requirements based on a mathematical model of the human glucose-insulin system.

The purpose of this study was to propose a possible structure to estimate the insulin level and to control the blood glucose level.

2. POSSIBLE CONTROL STRUCTURE

Very important for a control system is the possibility to estimate the necessary of insulin. For to reach this purpose, it is possible to use one of the next structures:

2.1. Neural Network Prediction Model

Using the neural network approach it is possible to compose a prediction model, very useful to test and validate the medical decisions [Iancu, 2004]. The structure is presented in fig. 1.
The neural network proposed to estimate the values of blood insulin concentration is feed-forward back-propagation network and it is organized in five layers, with 7, 5, 3, 2 and 1 neurons. The transfer functions used are:

- hyperbolic tangent sigmoid for the input and hidden layers.
- pure linear for the output layer.

The input of network is represented by the blood glucose level (measured). The output (target) is represented by the blood insulin level.

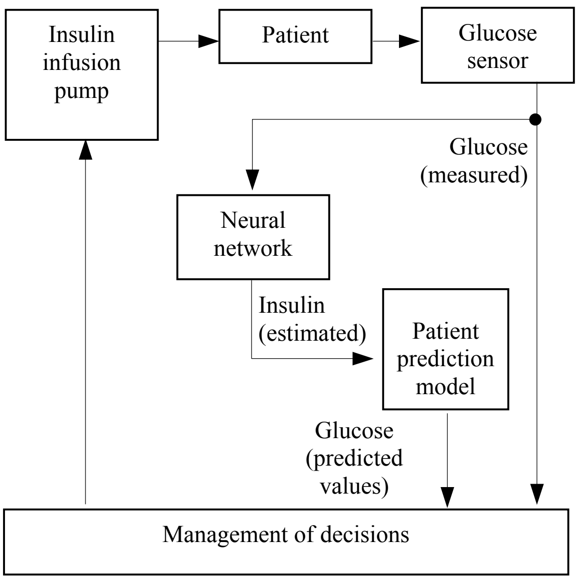

Fig. 1. The structure of adaptive blood glucose control using a neural network.

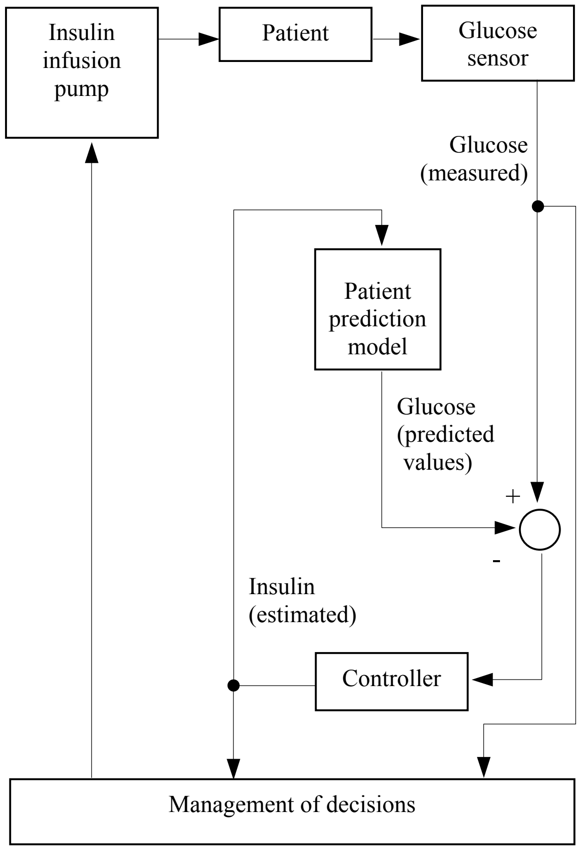

Fig. 2. The structure of adaptive blood glucose control using mathematical model.

The neural network is trained to reproduce the correspondent values of insulin when is known the glucose level, in accordance with the individual diabetes affection.

2.2. Prediction Structure Using Mathematical Model

Another possibility to estimate the level of insulin consists in utilisation of mathematical model. The structure of system is represented in fig. 2.
The patient prediction model reproduces, for an insulin level, the concentration of blood glucose. The level of insulin is modifying until the output of mathematical model (simulated value of glucose) is equal with the measured glucose (the real value from the patient). In this moment, the input in the mathematical model represents the estimated value for insulin blood level.
The management block receives the real value for glucose level, the estimate value for insulin level and, according to therapeutically program, command the pump.

3. MATHEMATICAL MODEL

For modeling the blood-glucose control system and a possible application of this to medical diagnosis we used the simplified structure of the physiological system. We accept for this the follows basic considerations:

- Blood insulin release increases proportionally to blood glucose concentration.
- Blood insulin inactivation is proportionally to the blood insulin concentration.
- The regulated variable is the blood glucose (concentration of glucose in extracellular fluids: blood and interstitial fluids).

We also used the simplifying assumptions:

- The liver releases in steady state the post-absorptive glucose and does not interfere in blood glucose control.
- The actions of glucagon, epinephrine and other secondary factors in blood glucose control were not account.
- The model ignores the peripheral glucose utilisation.
- The insulin is distributed uniformly in the plasma and interstitial fluids.
- The intracellular glucose can be neglect.

The equations of the mathematical model result from the preservation of material exchanges for glucose and insulin in system [Mountcastle, 1968]:

$$C\frac{dG(t)}{dt} = Q(t) - \gamma I(t)[G(t) - G_t(t)] - \delta[G(t) - G_t(t)] \quad (1)$$

$$C\frac{dI(t)}{dt} = -\alpha I(t) + \beta[G(t) - G_0] \quad (2)$$

The significance of variables are:

- $I(t)$ - insulin concentration in extra cellular fluids, measured in [mU%].
- $Q(t)$ - the absorption rate of glucose in blood stream.
- γ - proportionally factor between the insulin and glucose utilized in tissues.
- δ - proportionally factor for passive diffusion of glucose in tissues.
- C - volume of extra cellular fluids.
- $G(t)$ - concentration of blood glucose.

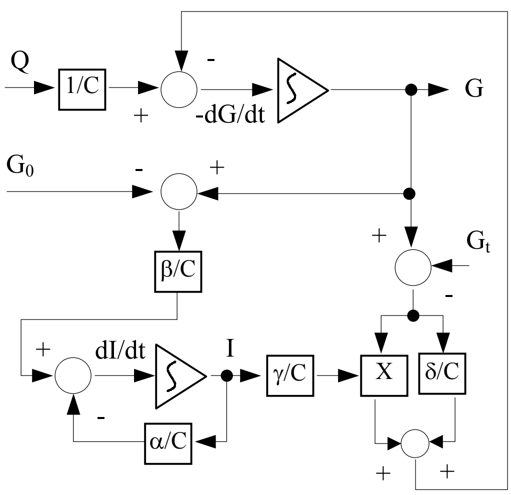

Fig. 3. The block diagram attached to the model.

- G_t - concentration of tissues glucose; we consider G_t=0 by initial absorption.
- G_0 - level of blood glucose above which insulin is released.
- β - proportionally factor relating glucose concentration to insulin release rate.
- α - proportionally factor relating insulin concentration to the rate of insulin inactivation by insulinase and/or anti-insulin antibody.

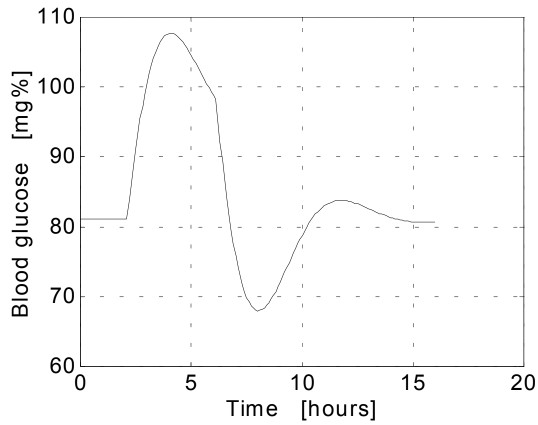

Fig. 4. Blood glucose evolution during glucose perfusion at healthy subject.

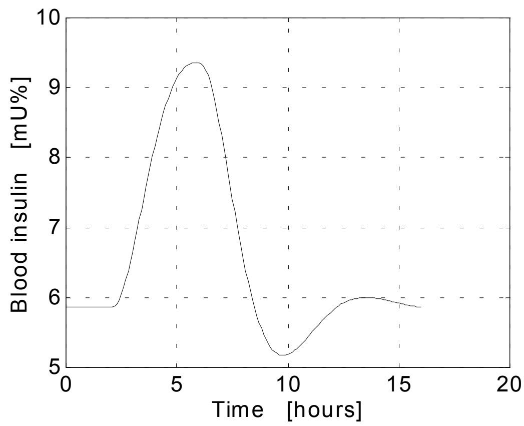

Fig. 5. Blood insulin evolution during glucose perfusion t healthy subject.

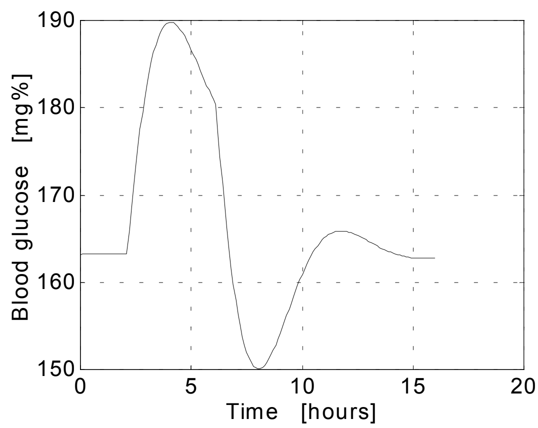

Fig. 6. Blood glucose evolution in diabetes patient.

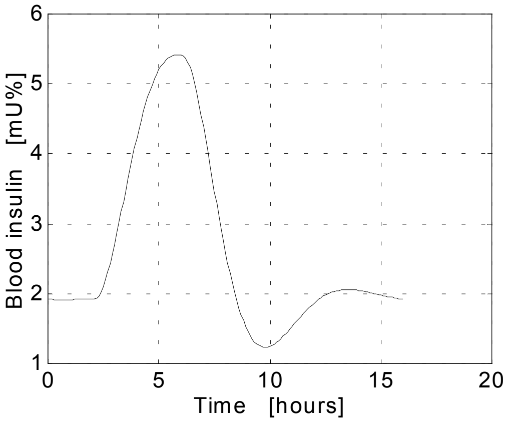

Fig. 7. Blood insulin evolution in diabetes patient.

In normal conditions, the blood insulin concentration is inaccessible parameter and the control of the infusion pump is very difficult. The results of simulation of glucose and insulin evolution during glucose perfusion (3g/kg-body/hour) are represented in fig. 4 and 5 [Iancu, 2003]. By the adecuate modification of the β - proportionally factor relating glucose concentration to insulin release rate, it is possible to simulate the behaviour of the mellitus diabetes patient. The results of simulation of glucose and insulin evolution are represented in fig. 6 and 7.

So, it is possible to know indirectly, the values of blood insulin and to control the infusion pump for insulin.

6. CONCLUSIONS

Using the mathematical model approach it is possible to compose a prediction structure, very useful to test and validate the medical decisions for healthy people, patients with melitus diabetes, pancreatic neoplasm or other physiopathological states without pancreatic desease. This methods could work as part of an artificial pancreas or could be part of the monitoring equipement in the intensive care services.

The results of this study can be applied also to other physiological systems, it offers important data for the medical practice and it contributes to introduce the computer-assisted diagnosis like a current medical method.

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