Fuzzy System-based Modelling of the Biological Regulator of Glycemia

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Abstract. Diabetes mellitus, illness related to a deficient regulation of glycemia, can cause serious complications in patients' health. Several artificial mechanisms for controlling glycemia exist, which try to replace the biological system. However, these mechanisms do not generally achieve an optimal control. We propose a specification of the biological glycemia regulation system, bearing in mind the knowledge given by experts and obtained from bibliography, and a regulating mechanism that complements to the biological system. For the design of the regulator, based on the control of glucose and insulin in blood, we propose a control system made up of different modules, where each one of them is put in charge of some type of substances that play a role in the glycemic control, and they are designed using fuzzy control structures. A collection of experiments has been carried out by means of a simulation of the proposed model, checking that fuzzy control provides good results for the studied cases.

1 Problem Exposition

1.1 Biological Problem

Glucose is an essential substance for cellular nutrition, especially for the muscular tissue and the brain, and its normal concentration (from a clinical point of view) is within the range of 70-120 mg/dl of blood. Hyperglycemia (high glucose level) as well as hypoglycemia (low glucose level) are dangerous for patients' health (glycemic coma, blindness, etc) [1, 2].

Pancreas is an organ that perhaps carries out the most important function related to the biological regulating mechanism of glycemia; the so-called hormone insulin (segregated by the pancreas) is the main regulator of the glycemic levels. On the other hand, when there is a hipoglycemic condition, another hormone called glucagon is produced, which stimulates the glycogenolysis or glucose release from the hepatic reserve. Insulin reduces glucose concentration in blood, facilitating the glucose absorption by target cells (muscular, cerebral, hepatic, etc.). A full or partial failure in insulin secretion causes the illness known as diabetes mellitus.

Other hormones influence on this regulating mechanism, such as adrenaline, but they have less incidence on it compared with insulin and glucagon. Moreover, other subsystems take part in this mechanism, such as the renal filter which eliminates the glucose excess in blood through the urine, when glycemia exceeds certain threshold.

1.2 The Problem of the Artificial Regulation

Most research in the field of diabetes is devoted to achieve an optimal metabolic control, by using artificial mechanisms of regulation that substitute or complement to biological regulating system.

The most usual artificial mechanism to regulate glycemia consists on the injection of several daily doses of synthetic insulin [2]. This therapy does not achieve a good control of glycemic level, because it is difficult to adapt the necessities of insulin throughout the day with punctual external supplies of it. Frequently, hypoglycemic episodes can appear in the very next hours to each injection, whereas the glucose level can be high lapsed several hours.

In order to adapt the insulin supply to the individual's necessities along the day and, therefore, to simulate more accurately the biological mechanism of glycemia regulation, a device called insulin pump has been designed [3, 4]. This device consists of an insulin reservoir, a catheter and a remote control system, in charge of giving the insulin quantities that have been previously programmed. Results of this therapy are quite positive, since the episodes of severe hypoglycemia practically disappear and the blood parameters are closer to normal values. However, some inconveniences associated to this treatment exist, like the risk that bears the surgical intervention for the subcutaneous installation of the device, and the feedback lack in the insulin infusion related to the glucose level. The necessity of a previous programming which implies a lack of autonomy in its functionality, leads to reflect on the possibility of designing an intelligent device that, according to the different detected glucose levels, was able to provoke the necessary actions to achieve a normoglycemic level.

2. Regulation Systems

In order to model the biological system we are studying, we have to consider how much each model fits the system features. The classic regulation models (PID type) have been widely studied and contrasted for being applied to linear systems or, in general, systems that are highly structured [5]. However, the dynamics of the system we deal with are not accurately known, which implies that the behaviour of a PID regulator and the derived results of its application could not be quite appropriate.

Models based on neural nets or genetic algorithms have the advantage of being able to be applied to poorly structured systems, from whom a knowledge base of relevant dimension is not a priori possessed. As a counterpart, we can point out the necessity to collect a wide set of empiric data which allows to infer regulation mechanisms based on the typical learning algorithms of these models [6].

Regulation models based on fuzzy sets are mainly applied to systems that have a knowledge base that could be virtually equal to the one a specialist has, where decisions are made depending on the combination of values of certain factors [6, 7, 8]. This would be the case of the system we are studying, so we will try to apply the fuzzy regulator features regulators to the problem of glycemia regulation. It is necessary to bear in mind that, in most cases, fuzzy models are complemented with neural or genetic methods which allow to modify the system of inference rules or other significant aspects as results are more and more accurately being obtained [9, 10].

3. Basic Problem Specification Oriented to its Fuzzy Design

In order to model this biological system, we will base on the following components:

- Pancreatic insulin provider subsystem (glucose elimination)
- Pancreatic glucagon provider subsystem (stored glucose release)

As explained before, one can find some other components or subsystems which participate in the glycemia regulation; however, they don't appear in this model because we consider that they would be a part of an external subsystem to the pancreas and that, in normal situations, their incidence in the regulation system is minimum [11, 12].

In table 1 glucose levels are divided into groups, determining different states:

Table 1. Glucose levels associated to the different metabolic states (L=low; M=medium; S=severe; VS=very severe)

Metabolic state	Normoglycemia	Hypoglycemia				Hyperglycemia			
Degree		L	M	S	VS	L	M	S	VS
Glucose (mg/dl)	70–110	65-70	60-65	50-60	< 50	120-140	140-250	250-300	> 300

It is necessary to keep in mind that the relationship between the amount of segregated insulin and glucose concentration in blood is not accurately known, although the function which relates both factors is considered to adopt the form of a sigmoid curve [1], just as shown in figure 1.

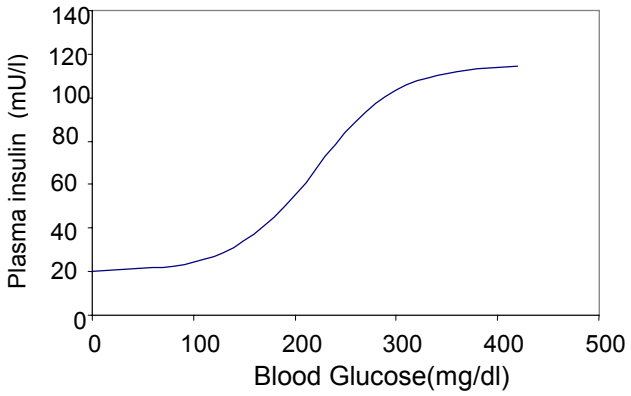


Fig. 1. Curve that relates the secreted insulin to the glucose concentration

We can observe that a basal secretion of insulin exists (that is, a minimum amount whatever the metabolic conditions are) and that it is around 25 miliunits per litre (mU/l).

For glucagon secretion, as it is an opposite insulin hormone, that is to say, it counteracts insulin action, it is frequent to relate both hormones [1, 13]. The function that would provide glucagon secretion, taking the secreted insulin as a parameter, would correspond to the curve shown in figure 2.

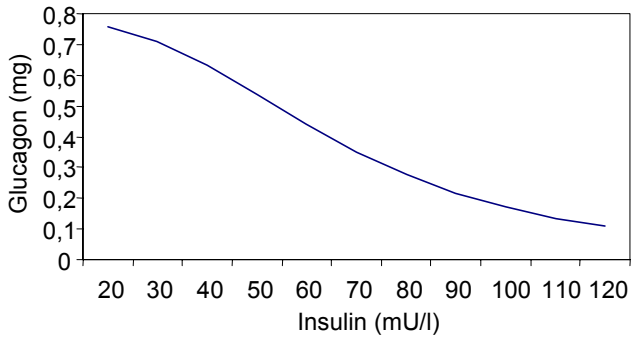


Fig. 2. Relation between secreted insulin and produced glucagon

Lastly, the relation between the amount of insulin and the metabolised glucose is considered to be expressed by means of a curve similar to that one shown in figure 3.

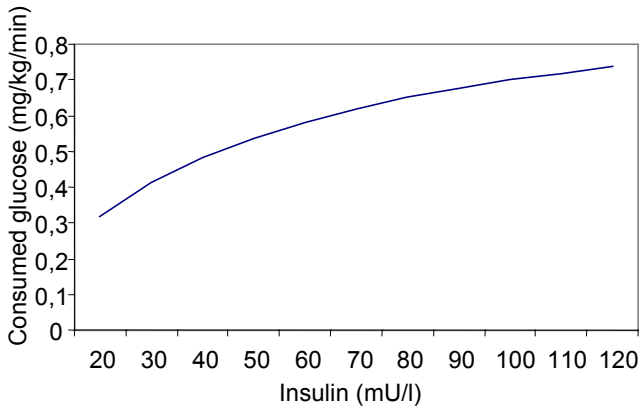


Fig. 3. Relation between secreted insulin and metabolised glucose

4. Fuzzy Design

In order to deal with the design of the glycemia regulating system, we can define three fuzzy subsystems: the first one would represent the relation between glucose concentration and amount of insulin that should be produced (*Insulin Producer*); the second one would correspond to the glucagon production depending on the insulin amount (*Glucose Producer*); the last subsystem would be related to the organism glucose consumption and the produced insulin (*Glucose Consumer*).

The first subsystem, *Insulin Producer*, accepts the variable G_{in} as an input, which represents the glucose concentration in blood (in mg/dl); it provides the variable I_{out} as an output, which corresponds to the amount of insulin, in mU/l, that should be supplied (naturally or artificially) to achieve the normoglycemic state.

The module called *Glucagon Producer* is defined by the input variable I_{out} ,which corresponds to the amount of this hormone, in mU/l, supplied to a patient; the output variable G_{add} corresponds to the quantity of glucagon secreted by the pancreas to counteract the insulin effects.

Lastly, the *Glucose Consumer* subsystem receives the variable I_{out} as an input, which represents the amount of insulin, in mU/l, supplied to the patient; it provides the output variable G_{sub} which corresponds to the glucose consumed by the organism as an answer to the presence of insulin.

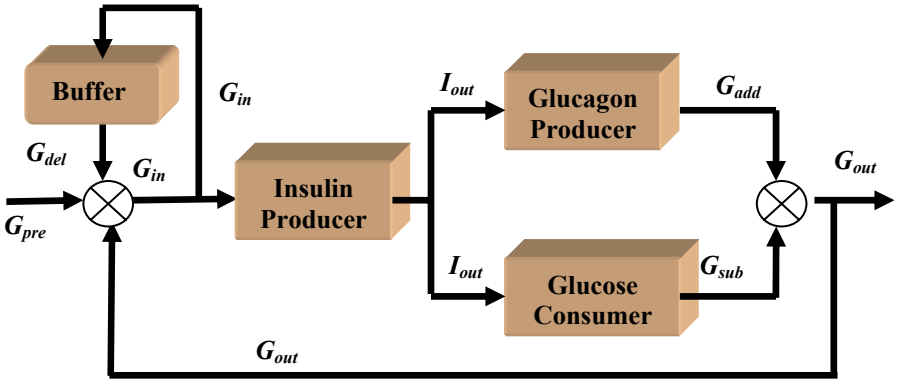


Fig. 4. Whole fuzzy system for blood glucose regulation

The whole system is shown in figure 4. Input G_{pre} corresponds to the previous supply of glucose, while the variable G_{out} represents the level of glucose after the complete process, where insulin is secreted (I_{out}), and this can cause glucagon production and consumption of glucose. The variable G_{out} feedbacks the system, being added to a new supply of glucose, so the addition of both is provided as an input (G_{in}) to the Insulin Producer subsystem (with a certain delay).

Once defined the operation model under normal conditions, we should focus on two different anomalous states: hyperglycemia and hypoglycemia; both states can be controlled by a compensating system that acts on these undesired deviations. Indeed, the biological regulating system can adopt abnormal behaviours within the diabetic casuistry, in which an external contribution of certain quantities of insulin covering the deficiency is needed.

At this point, we propose the design of a regulating system based on a compensating control which only acts in case of abnormal states. The architecture of the compensating system is showed on figure 5, in which a set of regulating modules are defined, connected in parallel to the subsystems which describe the model in figure 4. Each module is designed with the knowledge base generated by the production and insulin consumption curves under normal conditions, as well as the experience acquired in diabetes treatment (dose that can be supplied, temporary spaces supply-reaction, etc.). That is to say, it is necessary to define a set of rules that, besides identifying abnormal states, accurately compensate the detected deficiency. Because of that, we must count on an appropriate knowledge base given by a specialist, which can be used to design the regulator assuring that specifications are fulfilled. The system presented in figure 5 provides the design for implementing a regulating system that deals with the problem of automating the appropriate insulin dosage for diabetic patients.

5. Results.

The fuzzy model formulated in the previous point has been implemented using the Simulink® tool, integrated in the mathematical environment Matlab® from The MathWorks, Inc. Additionally, we have used the toolboxes Uitools and Fuzzy in order to develop a graphic management environment of the system and to model the proposed fuzzy subsystems, respectively.

The first set of experiments allows us to study the ability of the proposed system to achieve a normoglycemic level from a glucose concentration in blood above or below optimal limits. In figures 6 and 7, the system evolution is shown from a glycemic level of 200 and 300 mg/dl, respectively.

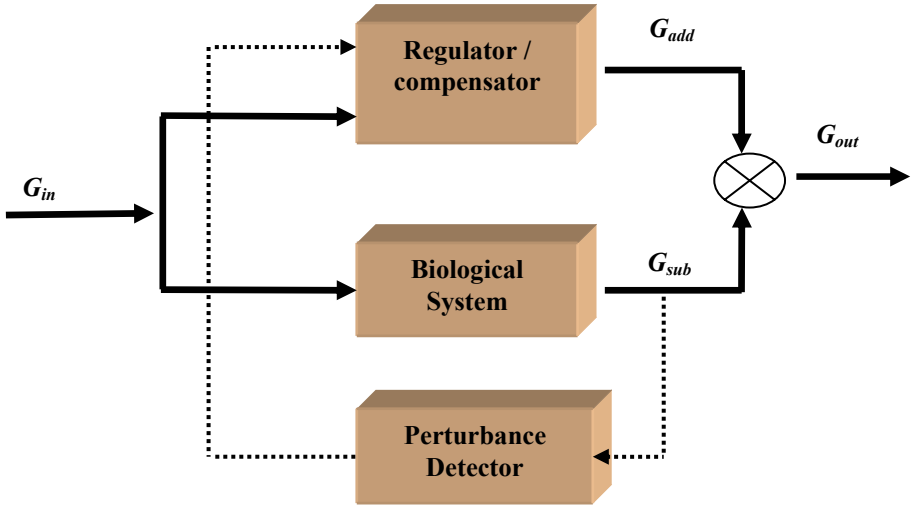


Fig. 5. Compensating system of the biological regulator

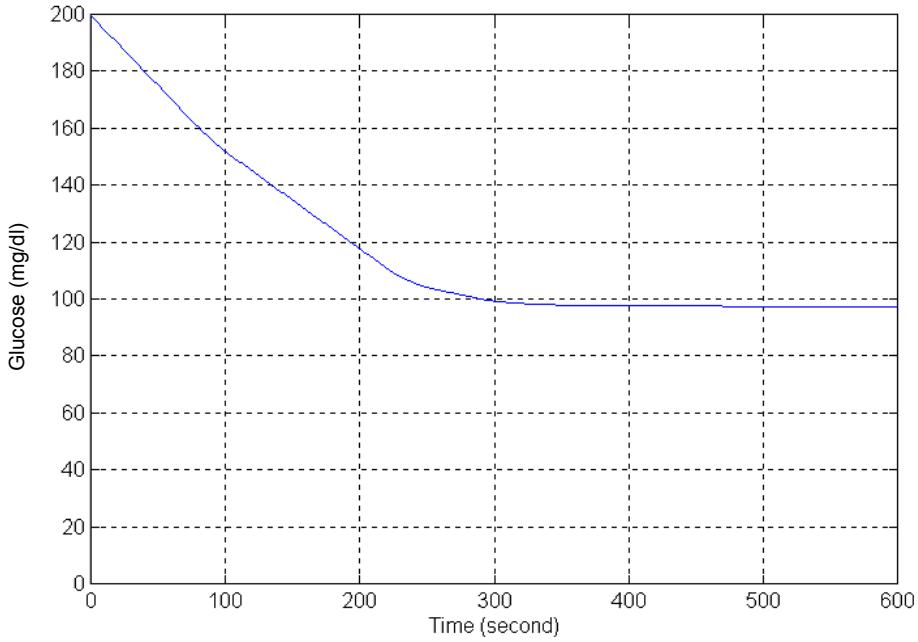


Fig. 6. Normalization of the glucose level from a concentration of 200 mg/dl

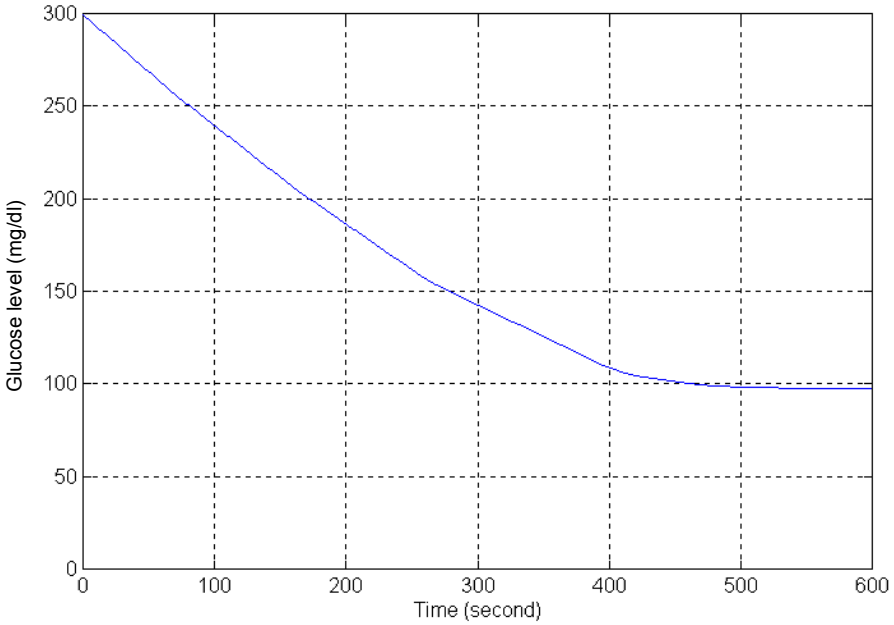


Fig. 7. Normalization of the glucose level from a concentration of 300 mg/dl

The second set of experiments is focused on the study of the system ability to return to a normoglycemic level when an instantaneous punctual distortion (that decreases or increases the glucose concentration) is introduced. Figure 8 shows the reaction of the system faced to the previously mentioned distortion where the glucose increases up to 200 mg/dl.

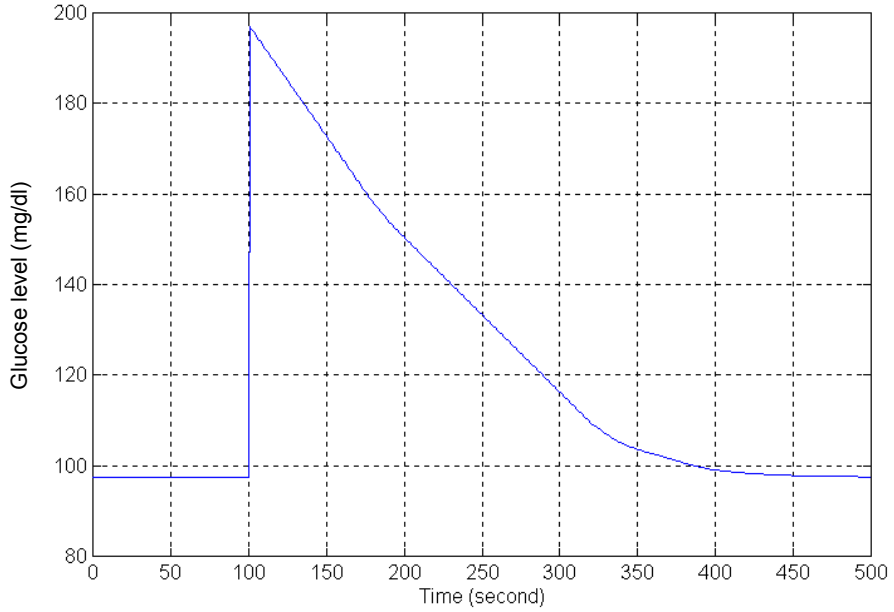
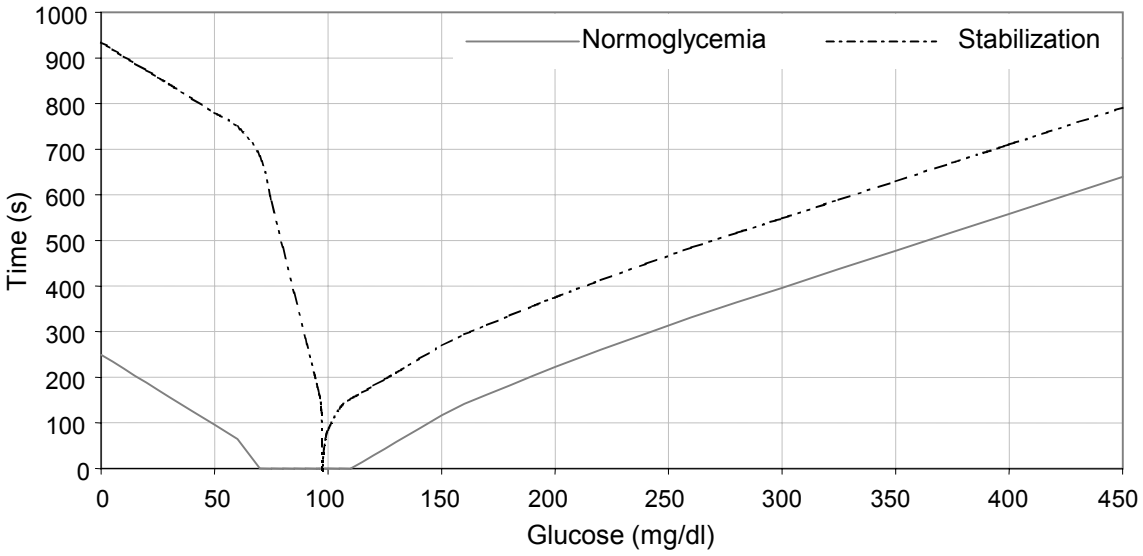


Fig. 8. Normalization of the glucose level considering a punctual increase up to 200 mg/dl

Figure 9 shows the results obtained with regard to the necessary time so that the system achieves the normoglycemia state coming from a hyperglycemia or hypoglycemia situation. A sample interval of 1 second



has been used.

Fig. 9. Necessary time to achieve normoglycemia and stability coming from different glycemic levels

6. Conclusions

We can observe how the application of control techniques based on fuzzy logic facilitates the implementation of regulating mechanisms for highly complex systems, affected by a high number of variables, some of them with a non defined behaviour. Most biological regulating mechanisms, and more specifically the one we deal with, belong to this set of systems. In this work, we propose the use of a fuzzy regulator to control glycemia, using a simulation implemented with modelling software.

A future work would consist of transferring the results obtained by means of the simulation to a hardware architecture [15, 16], so that the viability degree of the definitive installation in an electronic device of a fuzzy regulator, with the mentioned features in this text, could be widely studied. This task would imply the optimisation of the proposed design, as well as the addition of variables related to the glycemia regulating system whose influence in regulation is little and, therefore, they have not been considered in this first approach of the model [17].

Lastly, and in the long term, we can reflect on the development of an electronic device (or electromechanical, depending on its functionality) which can be implanted in human body and which supports to the biological glycemia regulating mechanism, also considering its use as a device for helping in diagnosis. This point would demand an interdisciplinary work because, besides the architectural design of the device, it would be necessary to study the biocompatibility of the used materials as well as the possible biological answers of human body to the presence of that electronic device.

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