Intelligent Insulin Pump Design

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***Abstract*—Diabetes Mellitus is a disease produced by a lack of insulin. In human beings, if insulin is not given externally, glycemia cannot be regulated correctly. According to several studies, tight control of glycemia reduces the chances of developing the ulterior complications of this disease. Automation of insulin infusion is one of the best ways of glycemic control. It is a goal searched from the 70´s when a first device was developed, the Biostator, a PID based automatic insulin infusion apparatus.**

Nowadays, this device is called "artificial pancreas". It is compound by a glucose sensor, a control algorithm, and an insulin pump infusion. Till now, control algorithms only could control glycemia around a basal value. Therefore, meal ingestion requires a manually added insulin dose called bolus.

Our group has developed several control algorithms that automatize the process completely without supplementary bolus requirements. They are based on differential geometric control techniques whose efficiency has been tested in a simulation environment. These techniques are based on feedback linearization and flatness based control. By these techniques, a nonlinear system becomes a linear and controllable one. In this work, a working prototype of insulin infusion pump is introduced to verify the efficacy of the control algorithms proposed.

Keywords— diabetes, pump, insulin, nonlinear control.

I. INTRODUCTION

Diabetes is a chronic disease that appears when the pancreas does not produce insulin, or the body cannot metabolize it properly. Insulin is one of the hormones that regulate the glucose in the body. Hyperglycemia is the result of a non-controlled disease. Over time, several organs like nerve system and blood capillaries are injured. In advanced stages of non-insulin-dependent diabetes (DMT2) or insulin-dependent diabetes (DMT1), the insulin infusion is required [1]. Even when there are several types of diabetes, this work is focused on insulin-dependent diabetes mellitus (DMT1) which requires the regular supply of exogenous insulin given the lack of insulin generation by the beta cell of the pancreas. The conventional therapy consists of the administration of exogenous insulin, several times in a day with tight glycemic control, but this cannot prevent its consequences effectively. As high is the glucose, higher is the risk of developing other diseases like retinopathy, stroke, diabetic foot, and other complications. National and international for diabetic prevention organizations like OMS or American Diabetes Organization prescribe the tight glycemic control, but this has associated a higher risk of hypoglycemia [2], [3]. An alternative to this method is the "bioartificial pancreas." In Argentina is being made a clinical trial with Langerhans islets encapsulated in alginate. This study used pigs free of porcine pararotavirus (PARV) from New Zealand. The islets with the capsules inside, injected into the peritoneal cavity, provide insulin to the body. Even when this technique seems to be promising, is affected by the low level of oxygen in the peritoneal cavity, altering the survival of the β cells. By other side, automation is becoming crucial for keeping safe the body low glucose levels. In this sense, automated continuous insulin infusion is better than manually insulin doses for prevention of events of hyperglycemia. This device is known as "artificial pancreas". It is made of a glucose sensor, a control algorithm, and an insulin pump infusion (Fig. 1).

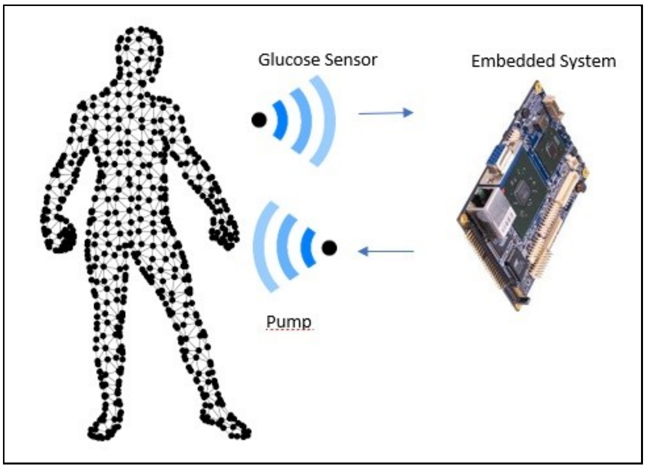

Fig. 1. Commercial insulin pump used in the initial tests.

II. NONLINEAR SYSTEMS DYNAMICS AND CONTROL

Nonlinear systems theory gives a conceptual framework for the understanding of physical systems as well as a better comprehension of their fundamental laws. In control systems practice, several components from different sources are used, mechanical, electrical, pneumatic elements, generally as a combination of them. Nevertheless, frequently, its first principles are considered as isolated concepts, without almost any link between them. Control theory lets to see the similarities between dynamic structures that, apparently have nothing in common between them. For instance, some issues, traditionally considered as electrical problems, such as electrical motor control, could be advantageously studied from the nonlinear dynamic theory. Problems to solve in this

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case have to do with non-measurable variables such as electromagnetic flux in the air gap and others, required to achieve effective control of the plant. In this sense, differential geometric control techniques developed by Isidori, Sartry, and others [4] are helpful for control systems design. Using feedback linearization, by a change of coordinates, called diffeomorphism, a nonlinear system can become a linear and controllable one.

Nevertheless, its sensitivity to parameters variability makes it susceptible to lose the exact cancellation of nonlinearities resulting in a less robust control technique. The theory of flatness can be helpful to solve this problem. Flatness theory had its roots in the works of Cartan and D. Hilbert, related to a class of sets of differential equations, but the application to control systems was made by Fliess, Levine, Martin, and Rouchon [5]. They introduced it in 1992, and soon it became in a branch of nonlinear control theory with applications in industry. A nonlinear system is flat if, it is possible to find out a set of output variables, called flat outputs, such the system is (differentially) flat over the differential field, generated by the flat outputs. In flatness theory, flat systems can be considered as an extension of linear systems even when the control techniques used are entirely different. The flatness property was defined by first time by Fliess in the context of dynamical systems, and the term flat is used in the sense that the flat outputs are similar to the coordinate planes in the Frobenius theorem in differential geometry. Dynamical systems that fulfill the flatness property are those whose integral curves can be mapped in an injective way into algebraic curves. This property let planning the trajectories of nominal solutions efficiently than with other control techniques. It means that if the dynamical model of the system can fulfill the necessary conditions, then the control problem can be simplified enough to obtain its essential core becoming flatness property into a powerful control technique.

This property let planning the trajectories of nominal solutions efficiently than with other control techniques. It means that if the dynamical model of the system can fulfill the necessary conditions, then the control problem can be simplified enough to obtain its essential core becoming flatness property into a powerful control technique. The term flatness does not describe a specific control algorithm but a generic point of view for control system design. Flatness control theory can be developed using different mathematical tools like Lie- Bäcklund transforms and differential geometry of jets and prolongations of infinite dimension. It is also closely related to exact linearization, and it is possible to say that every system that admits exact linearization is flat and vice-versa [6], [7]. The concept of endogenous feedforward is the link between feedback linearization and flatness and add robustness making the control implementable in a practical sense.

III. DIABETES MELLITUS

The evolution of insulin pumps and continuous glucose sensors technology has progressed a lot from the days of the Biostator; the first practical equipment developed for glucose control [8]. However, the glucose homeostasis depends on a numerous amount of hormones difficult to estimate and then, there are still several problems to solve before a fully practical device reach the maturity safely for a fully automated operation, without any operator intervention. From a process instrumentation point of view, it is possible to measure only the intravenous (IV) or subcutaneous glucose (SC) but the glucose system uses an enormous amount of hormones, like glucagon for instance but exercise or stress also affects the cell glucose metabolism or its liberation from the liver. Therefore, using "based model control", with non-measurable variables requires the development of "state observers".

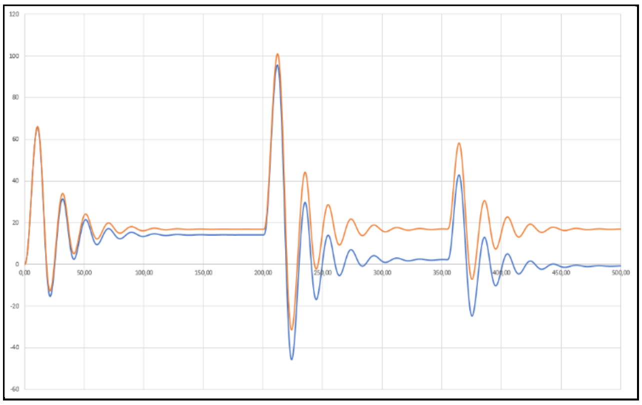

Fig. 2. Output of the insulin pump compared with simulations, first tests.

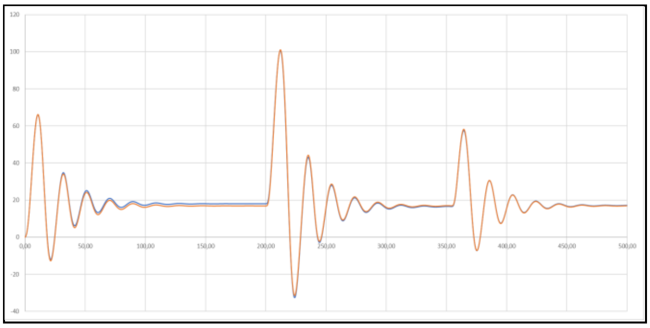

Fig. 3. Output of the insulin pump compared with simulations.

Another problem is the non-physiologic path of the insulin [9]. The pancreas secretes insulin directly into the portal artery while using a subcutaneous path requires to consider the delay in the insulin action to reach the extra cell tissue. This time delay varies from person to person, and even in the same subject, it is variable along the day and depends on other variables like type of exercise and type of meal ingested. There are also a group of patients whith glucose level swings quickly from high to low and from low to high. This condition is called "labile" diabetes. These difficulties make hard the algorithm design because an insulin overdose could lead to a hypoglycemic episode. Hypoglycemia leads to loss of consciousness and even death. About continuous glucose monitoring, there are problems of exactness and dispersion in measurements. These problems affect mainly the measures in the basal range of glucose with the risk of hypoglycemia. In night fasting conditions, the cells metabolize glucose mainly by the nervous tissue without insulin mediation. This metabolization depends on the gradient between the extra and intracell glucose concentration. This situation makes the system extremely nonlinear raising a challenge to the practical implementation of this kind of devices. These problems are the reason why there are so few commercially available devices developed [10].

There also exist commercially available insulin pumps but require its programming by the user and therefore, patient-dependent. This project proposes an insulin pump development at a lower price than others existing in the commercial market. At the same time, implement a control algorithm that avoids the manually added pre-meal bolus. That is a fully automated device. In Argentina, there is an insulin dependent diabetic population of around 400,000 people. These people have a poor diabetes monitoring and a high risk of developing complications sometimes deadly. An automated insulin pump could help to prevent these problems enhancing the life quality of these people and, at the same time develop high tech devices able to reach international markets. There are direct and indirect benefits from this proposal:

Direct benefits

- Insulin-dependent diabetic people in Argentina: 400, 0000.
- Labile diabetic people in Argentina: 40, 000.

Indirect benefits

- It will reduce costs in the budget of the national health system (basically, preventing the diabetes complications).
- It enhances the route of national industry to progress towards new developments.
- It helps Universities to develop high-tech policies.

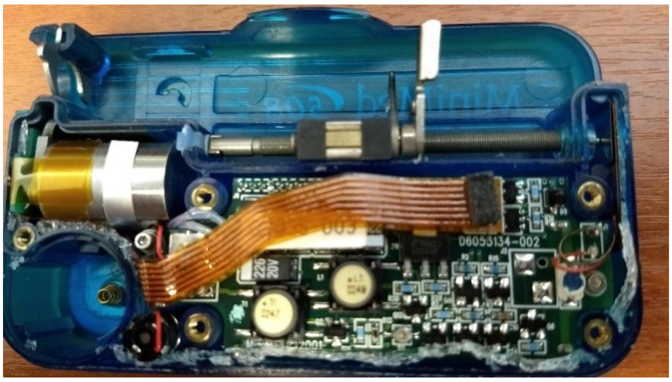

Fig. 4. Commercial insulin pump used in the initial tests.

IV. Conclusions

This project is the integrator of “Nonlinear motor control for biomedical applications”, which is developing new algorithms for glycemic control avoiding hypoglycemia and software apps to develop an artificial pancreas.

The software developments use differential geometry techniques like feedback linearization and flatness, already developed by the authors [11], [12]. They can compensate for noise and uncertainties from an unknown environment, time variant biological parameters and other aspects not considered in the mathematical models of the disease. Besides, it has been developed dynamical simulations where the algorithms are tested in a noisy environment and time delays in glucose monitoring and insulin action. Also, a monitoring and control system for DMT1 treatment, by design a prototype of insulin infusion pump with wireless communication and an intelligent phone as a man-machine interface is being developed. Information register will be made from the mobile phone to a web server, patient access and developed with high-security characteristics. The methodology of working is based on the analysis of mathematical models of the disease and identification of parameters, the development of a Bergman Minimal Model discretized for the validation of the designs already done. It went on with the design of new control strategies, its numerical simulation and by last, its multidisciplinary discussion.

A prototype of an insulin pump is being constructed [13]; it is used to validate the control algorithms experimentally already developed (Figs. 4 and 5). The results are also being contrasted with clinical data from studies like the intravenous glucose tolerance test (IVGTT) and data samples from glucose measurements done in the School of Science and Technology, University of San Martín. In this first phase, step and dc motors with hardware Arduino and an electromechanical system ad hoc are being developed (Figs. 2 and 3).

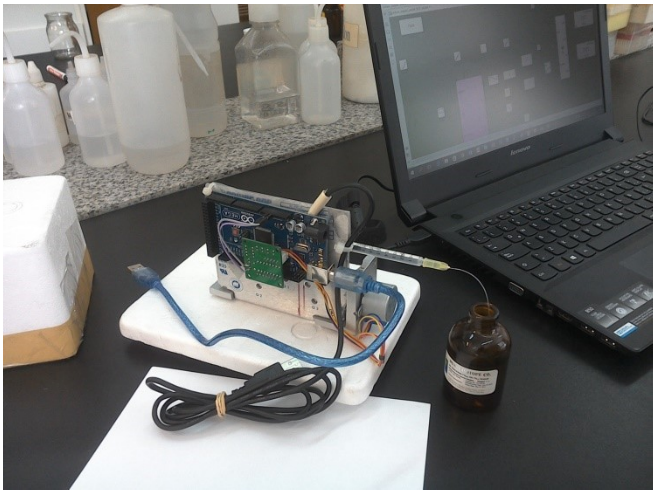

Fig. 5. Arduino prototype used in the initial tests.

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