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An adaptive backstepping based non-linear controller for artificial pancreas in type 1 diabetes patients

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ABSTRACT

Artificial pancreas enables closed loop automated control for blood glucose regulation in type 1 diabetic patients. Simple backstepping controller for regulation of blood glucose level has recently been proposed in the literature. In this research work, we have proposed backstepping based adaptive controller for integration in artificial pancreas. Controller design has been based on Bergman's minimal model which represents the dynamics of blood glucose-insulin system of human body. Glucose effectiveness factor has been treated as an unknown parameter and its value has been adapted using Lyapunov based adaptive backstepping control approach. Effects of meal disturbance, physical non-linearities and sensor noise have also been considered in the controller design. A complete mathematical derivation of the proposed nonlinear controller has been described and simulation results have been presented using Matlab/Simulink environment. Results indicate improvement in tracking response and overshoot/undershoot characteristics as compared to some recently developed techniques in literature. Proposed controller assures dynamic stability against disturbances and deviations in human body parameters. Practical implementation of the proposed controller can result in better artificial pancreas.

1. Introduction

Diabetes is a widespread disease. Each year, billions of dollars are spent on its treatment. In year 2002, total medical expenses on the treatment of diabetes in US were estimated to be $ 132 billion which exceeded to $ 245 billion by 2012 [1,2]. Studies also indicate that the number of diabetic patients worldwide may increase to 300 million by year 2025. This number was much less back in 1995 with 135 million patients [3]. This bleak situation has motivated many researchers to look for new methods and ways of improvement in treatment of diabetes.

Type 1 diabetes is characterized with hyperglycemia in which a patient has high blood glucose level due to lack of insulin in the body. Because of the absence of pancreatic beta cells, insulin produced by pancreas is not sufficient to maintain glucose concentration to the normal level. It is different from diabetes type 2 in which the body is resistant to insulin action [4].

All the biological processes in a human body are complex and non-linear in nature. Body parameters are subjected to variations. In diabetic patients, blood glucose level is required to be carefully tracked. If blood glucose level remains high for prolonged periods, it can cause damage to eye retinas, kidneys and nervous system. In contrast, insulin overdose can lead to hypoglycemia; a condition of low blood glucose level; which can result in seizures, coma or even death [5].

Insulin is externally injected to overcome its deficiency in diabetic type 1 patients. Manual injection of insulin is the most common and cheapest form of treatment. In contrast to manual injection, automated infusion offers several advantages. Artificial pancreas is developed for automated infusion of insulin in the human body. It eases out the patient's life style by maintaining a better and stress-free health.

Artificial pancreas enables closed loop control for blood glucose regulation. OGTT (Oral Glucose Tolerance Test i.e. ingesting glucose by mouth), IVGTT (Intravenous Glucose Tolerance Test i.e. injecting glucose into body) and MMTT (Mixed-Meal Tolerance Test i.e. taking a dose of mixed meal by mouth) are few of the tests designed to evaluate the performance of artificial pancreas [6]. In each test, the response of a controller against an external glucose as an input is studied by frequently taking blood samples and checking insulin resistance over a period of time. The measure of effectiveness of a controller to be used in an artificial pancreas can be examined by convergence time to different glucose set points, overshoots/undershoots from the set points and steady state error.

In order to fully rely on artificial pancreas, it is required to make its performance robust and dynamically stable. Robustness and sta-

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bility of a system explicitly depend on its integrated controller. For artificial pancreas, several control techniques and algorithms are available in literature. Proportional-integral (PI), linear quadratic regulator (LQR), model predictive control (MPC) and fuzzy-PI are some of the linear controllers proposed for artificial pancreas [7,6,8–12]. H-infinity based controllers provide better robustness characteristics among linear controllers [13]. Dynamics of blood glucose-insulin system are generally non-linear in nature. Linear controllers are applicable only on linearized models. Linearization of a practically non-linear system limits the applicable range of a controller. Large disturbances and abrupt parameter deviations dominate due to the presence of non-linearities within the system. Under such situations, performance of linear controllers quickly degrades and a system may lead to instability.

In contrast to linear controller, non-linear controllers offer better dynamic stability and are robust. Such controllers are ideal for complex, dynamic and non-linear processes of human body. They successfully compensate the effects of system non-linearities and parameter deviations which are generally neglected by linear controllers [14,15]. In [16], a non-linear controller based on super-twisting sliding mode control (SMC) technique has been presented for artificial pancreas. Although SMC is insensitive to model mismatches and parameter deviations, but it is accompanied by an unavoidable phenomenon of chattering. Physical actuators within artificial pancreas are susceptible to unwanted noise and malfunctioning due to chattering in the control input [17]. In [18], a backstepping based non-linear controller has been presented for artificial pancreas. This controller has claimed lesser convergence time and improved dynamic response in comparison to linear controllers.

Scope of non-linear control theory is yet more to be explored for artificial pancreas. In this research work, an adaptive backstepping based non-linear controller has been designed for artificial pancreas and its stability analysis has been done using Lyapunov stability theory. Control design is based on minimal model of blood glucose-insulin dynamics proposed by Bergman [19]. It is a physiologically verified three states model with identifiable parameters. To make our controller adaptive we have considered "Glucose Effectiveness Factor" (later described as parameter p_1) as an unknown parameter. This approach is more practical because glucose effectiveness factor can vary from patient to patient or sometimes for the same patient.

Response of the proposed controller has been evaluated in Matlab/Simulink environment. Comparison of the proposed controller has also been made with some other control techniques available in the literature and simulation results have also been discussed in detail. Simulation results and the analysis for the nonlinear controller design indicate that the proposed controller has potential to improve the efficiency of the artificial pancreas.

The remaining part of the paper has been organized as follows: Section 2 briefly reviews mathematical models representing blood glucose-insulin dynamics of human body. Complete mathematical derivation of the proposed controller has been presented in Section 3. Simulation results have been discussed in Section 4 and conclusions drawn from simulation results have been given in Section 5.

2. Mathematical representation of glucose-insulin dynamics

In human body, glucose concentration in blood is mainly regulated by liver and pancreas. Through interaction of these two organs, low and high glucose concentrations are controlled by producing glucose and insulin in body as elaborated in Fig. 1.

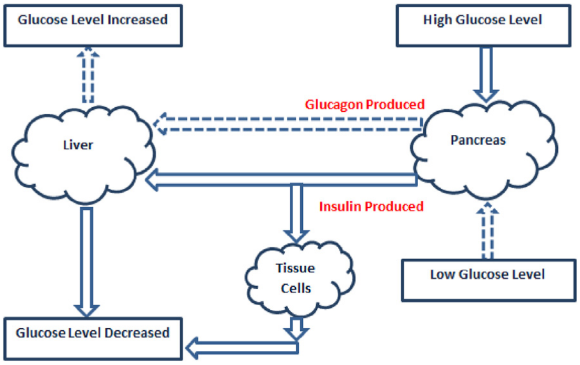

Fig. 1. Glucose regulation in human body.

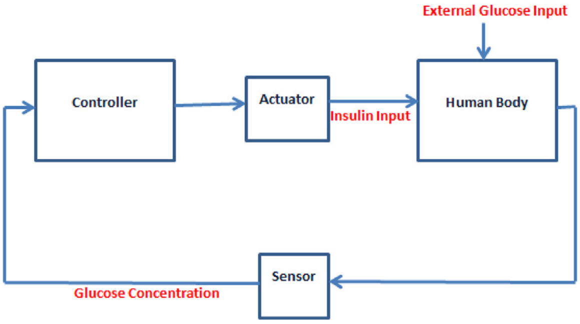

Fig. 2. Closed loop control of blood glucose.

For controller design, mathematical models describing glucose-insulin dynamics of human body are always required [20]. Fortunately, researchers have presented various models quite before the advent of modern controllers. Bolie (1961) and Ackerman et al. (1965) proposed linear models for glucose-insulin dynamics [21,22]. These models comprise of only two states. Tiran et al. (1979), Sorensen (1985), Hovorka et al. (2004) and DallaMan et al. (2007) proposed more comprehensive yet complex mathematical models [23–25]. These models show nonlinear nature of glucose-insulin dynamics. Bergman et al. (1981), Cobelli and Mari (1983) and Lehmann (1992) proposed minimal models to describe glucose-insulin dynamics of human body [26,27]. Minimal models are simpler encompassing all relevant parameters with reduced number of state variables [19].

An authentic model can be used to design different control algorithms which might be helpful for technological developments in the field of biomedical engineering. A simplified closed loop feedback system is shown in Fig. 2, which shows a sequence by which blood glucose level is regulated automatically with a controller. A sensor measures glucose in blood and gives an electrical signal to controller which releases insulin slowly into the body through an actuator.

A nonlinear model for blood glucose-insulin system is given by the following Eqs. (1)–(3). This model has been derived from the work of R.N. Bergman and often referred to as Bergman's minimal model of blood glucose-insulin dynamics [28]. It is a physiologically verified three state model with identifiable parameters. This model takes into account the effect of glucose effectiveness in human body and delay in insulin action.

$$\frac{dG}{dt} = -p_1 G - X(G + G_b) + \frac{G_{meal}}{V_1} \tag{1}$$

$$\frac{dX}{dt} = -p_2 X + p_3 I \tag{2}$$