

# Chaotic Dynamic Analysis and Nonlinear Control of Blood Glucose Regulation System in Type 1 Diabetic Patients

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**Abstract:** In this paper, chaotic dynamic and nonlinear control in a glucose-insulin system in types I diabetic patients and a healthy person have been investigated. Chaotic analysis methods of the blood glucose system include Lyapunov exponent and power spectral density based on the time series derived from the clinical data. Wolf's algorithm is used to calculate the Lyapunov exponent, which positive values of the Lyapunov exponent mean the dynamical system is chaotic. Also, a wide range in frequency spectrum based on the power spectral density is also used to confirm the chaotic behavior. In order to control the chaotic system and reach the desired level of a healthy person's glucose, a novel fuzzy high-order sliding mode control method has been proposed. Thus, in the control algorithm of the high-order sliding mode controller, all of the control gains computed by the fuzzy inference system accurately. Then the novel control algorithm is applied to the Bergman's mathematical model that is verified using the clinical data set. In this system, the control input is the amount of insulin injected into the body and the control output is the amount of blood glucose level at any moment. The simulation results of the closed-loop system in various conditions, along with the performance of the control system in disturbance presence, indicate the proper functioning of this controller at the settling time, overshoot and the control inputs.

**Keywords:** Chaos, Glucose-Insulin Blood System, Lyapunov exponent, Sliding Mode Controller, Fuzzy Logic.

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## I. INTRODUCTION

Diabetes is one of the most common and most destructive chronic diseases in the world, which Until now, definitive therapies have not been identified and the patient will endure the illness until the end of his life. For this reason, it is necessary to organize a regular program to deal with its complications. The malignant nature of diabetes is that if it is not detected and controlled in a timely and correct way, it can threaten the health of various organs of the patient.

In recent years, many studies have been conducted on diabetes and its control. Here are some examples of studies done on diabetic patients in general. In 1979, Cobelli and colleagues presented a comprehensive non-linear model for studying the short-term glucose regulation system [1]. In 1984, Salzsieder and colleagues argued that in order to control the long-term regulation of blood glucose, control parameters for each diabetic patient should be estimated separately [2]. In 1984, Wolf and his colleagues presented an algorithm to estimate the positive Lyapunov exponents from an experimental series of times [3]. In 1986, Wolf observed the phenomenon



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of chaos with the Lyapunov exponent's function [4]. In 1991 Fischer utilized the Bergman Minimal Model to minimize the difference in the concentration of blood glucose from a natural value using the objective function of the error-squared integral [5]. In 2001 Mendel introduced a fuzzy logic-based uncertainty system [6]. In 2002, Chase presented a proportional derivative controller using the Bergman model to control the level of diabetes in diabetic patients [7]. In 2003, Yoneda and Iokibe have been predicting blood glucose based on chaos and insulin regulation for diabetic patients [8]. In 2004, Ibbini and his colleagues proposed a close-loop optimal control method for the development of the Bergman model to improve the blood glucose status in diabetic patients [9]. In 2004, Katayama and Sato also investigated the blood glucose prediction system by chaotic method [10]. In 2006, Parisa Kaveh studied high-order sliding mode control for the blood glucose system [11]. In 2008, Parisa Kaveh, has regulated blood glucose system by a double-acting high order sliding mode controller [12]. In 2013, Sudabeh Taqian has presented a high order sliding mode controller by setting a fuzzy control signal constant [13]. In 2013, Kichler and his colleagues described the relationship between hemoglobin A1C in adolescents with type 1 diabetes mellitus with family-related chaos phenomena [14]. In 2014, Carlos examines that the biological diversity of glucose and insulin is a definitive component of chaos [15]. In 2015, Emanuel explored the parameters of the Bergman model on diabetic mice [16]. In 2016, Li Wenshi and Feng Yejia have investigated non-invasive blood glucose measurements based on chaotic analysis [17]. In the same year, Kostanzo her colleagues reviewed the evolutionary pattern of blood sugar in type 1 diabetic patients based on the phenomenon of chaos [18]. In 2017, Abdullah Idris Enagi and his colleagues presented a deterministic mathematical model of the diabetes mellitus disease [19]. In 2018, Sh. Asadi, and V. Nekoukar, presented an adaptive fuzzy integral sliding mode controller for BGL regulation in patients with type 1 diabetes [20]. In 2018, H. Heydarinejad and his colleagues proposed a combination of fractional order nonlinear control and sliding mode observer for blood glucose regulation in type 1 diabetes mellitus. [21].

In this research, in the first step, the behavior

of time series was derived from patient sampling by Lyapunov exponent method which used Wolf's algorithm and also the power spectral density method has been evaluated and their chaos was reviewed and confirmed. In the second step, the Minimal Bergman model is used in order to the modeling of these time series. Also, to validate this model was compared with input data and its error analysis was studied and finally a fuzzy high-order sliding mode controller (FHOSMC) was designed to control the amount of insulin injected to the patients. In this paper, by presenting a novel method of a fuzzy inference system, in order to improve the control method presented in [11], to obtain constant values in a high-order sliding mode controller, this controller performs better than the above-mentioned high-order sliding mode controller.

## II. CHAOTIC DYNAMICS ANALYSIS OF BLOOD GLUCOSE-INSULIN SYSTEM

In this paper, the dynamics analysis of blood glucose-insulin system is based on data from blood glucose collected from a healthy person and diabetic patients. A healthy person is a 22-year-old man and three types 1 diabetic patient, who are an 18 years old man, a 20 years old man and a 22 years old woman, respectively. The data are collected from a medical-sports center. Also, these patients are differentiated by their body initial conditions, such as different nutrients and different levels of primary glucose are distinguished. Plus, to consider different physical characteristics of their bodies, different body parameters have resulted.

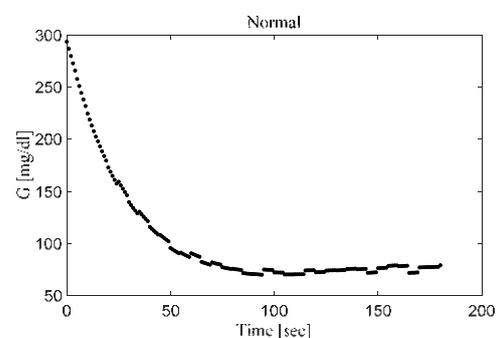


Fig. 1. Blood glucose of a healthy person

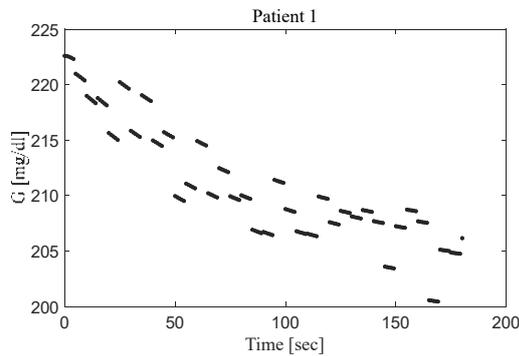


Fig. 2. Blood glucose of patient 1

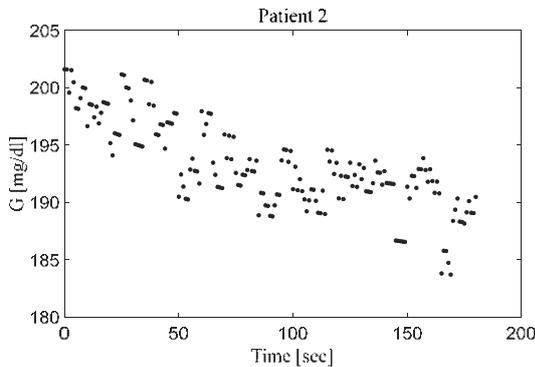


Fig. 3. Blood glucose of patient 2

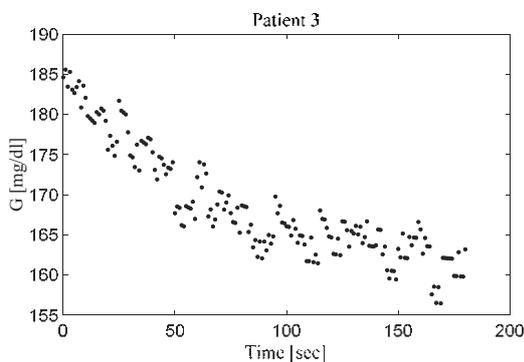


Fig. 4. Blood glucose of patient 3

It should be noted that these data are measured in the following way. In the beginning, 0.3 glucose unit was injected into the patient and the healthy person. During the 180 minute period, the blood glucose level of these people was measured and recorded. Time series for a healthy person and patients are in Figs. 1 to 4. Also, to prove the chaotic behavior of these data, the Wolf algorithm is used to calculate the Lyapunov exponents function and the power spectral density method.

As shown in Fig. 1, the healthy body, even though injected glucose in the first moment, secreted insulin and decrease blood glucose level naturally to the normal range of 70, but it can be seen in Figs. 2 to 4, the first patient's glucose level is in the range of 205 and the second patient is in the range of 190, and the third patient is in the range of 160 and their body cannot secrete the insulin which is required.

The nature of chaotic systems is irregular responses and stochastic states in time series, which, as shown in Figs. 1 to 4, these clinical data are chaotic. In order to illustrate this chaotic behavior, the Wolf method is used to calculate the Lyapunov exponents and the power spectrum density method.

Wolf's method is one of the most common methods for calculating the Lyapunov exponent. In this study, (1) is used to calculate the largest positive Lyapunov exponent:

$$\lambda_1 \approx \frac{1}{N\Delta t} \sum_1^{M-1} \log_2 \frac{L_i^\circ}{L_i} \tag{1}$$

$$N\Delta t = t_n - t_0$$

Where  $M$  is the number of times that the loop is executed and repeated.

TABLE I  
LYAPUNOV EXPONENT OF THE TIME SERIES OF THE WOLF METHOD

Patient 3	Patient 2	Patient 1	Healthy person
$3.75 \times 10^{-4}$	$18 \times 10^{-4}$	$4.05 \times 10^{-4}$	0.000235

If the Lyapunov exponent contains negative numbers, it indicates the existence of a constant equilibrium point in the nonlinear dynamical system. If the Lyapunov exponent is zero, it indicates that the distance between the trajectories is constant. Ultimately, the positive values of the Lyapunov exponent are chaotic nonlinear dynamics. The values obtained in Table I indicate that the Lyapunov exponent is positive. The positive of these exponents indicate the chaos of the time series.

The Power Spectral Density Function (PSD) shows the power of system energy changes in terms of frequency based on the Fourier series. In other words, this function shows at which frequencies the changes are strong, and at which frequencies the changes are weak. This function is obtained by (2) [6], [22] and [23].

$$\hat{x}(\omega) = \frac{1}{\sqrt{T}} \int_0^T x(t) e^{-j\omega t} dt \tag{2}$$

$$S_{xx}(\omega) = \lim_{T \rightarrow \infty} E[|\hat{x}(\omega)|^2]$$

In Figs. 5 to 8, the PSD is observed for the healthy person and diabetic patients:

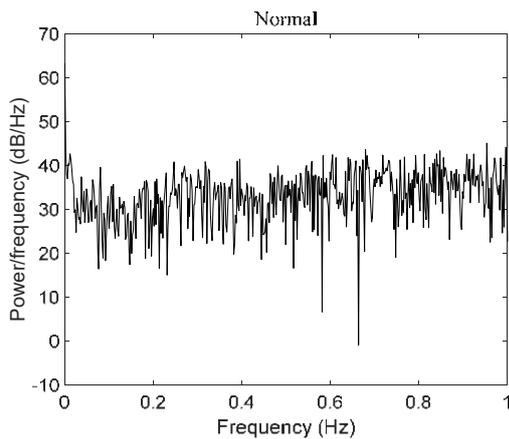


Fig. 5. Power spectrum density of the healthy person

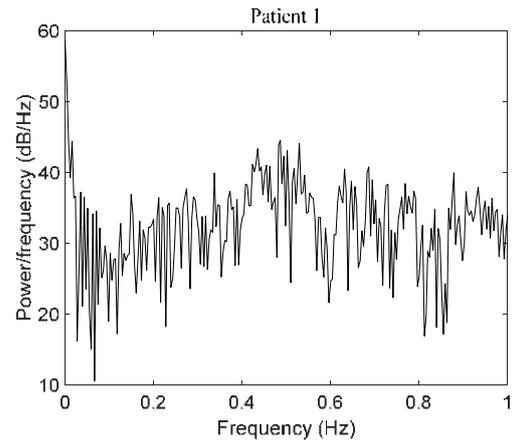


Fig. 6. Power spectrum density of patient 1

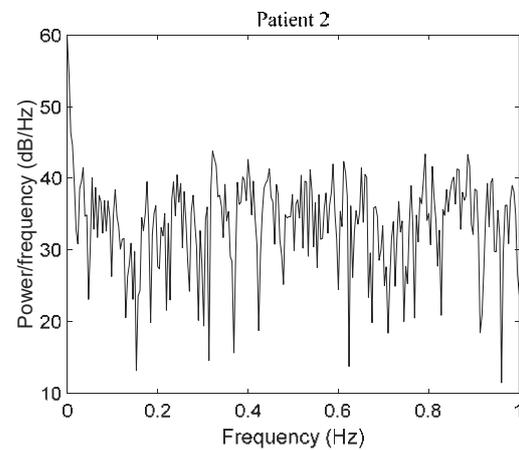


Fig. 7. Power spectrum density of patient 2

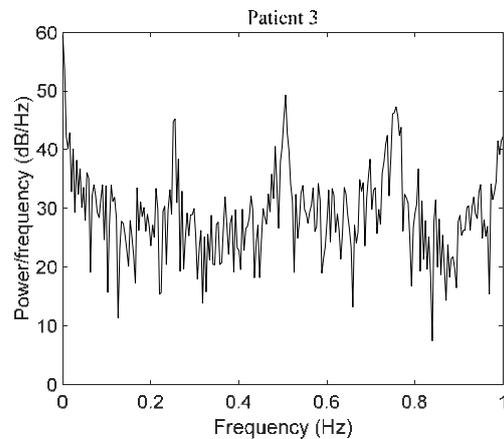


Fig. 8. Power spectrum density of patient 3

Due to the wide spectrum of frequency in the PSD function for the healthy person and the patients, chaotic behavior of the time series signals is proved.

### III. MATHEMATICAL MODELING OF BLOOD GLUCOSE SYSTEM

The Bergman Minimal Model is a non-linear model that describes the relationship between glucose-insulin in the human body. This model is a very common model in research related to the analysis of blood glucose systems. The main advantage of this model is the simplicity of the structure, the ability to estimate the physiological parameters of the model using blood glucose and plasma insulin, which is obtained using Clinique data. The Bergman blood glucose dynamics is represented by (3) [11]:

$$\begin{aligned} \dot{G}(t) &= -p_1[G(t) - G_b] - X(t)G(t) + D(t) \\ \dot{X}(t) &= -p_2X(t) + p_3[I(t) - I_b] \\ \dot{I}(t) &= -n[I(t) - I_b] + \gamma[G(t) - h]^+ t + u(t) \end{aligned} \quad (3)$$

In the above equation,  $G(t)$  is blood plasma glucose concentration ( $mg/dl$ ),  $X(t)$  effect of insulin on the net glucose disappearance ( $1/min$ ) and  $I(t)$  is the insulin concentration in plasma at time  $t(\mu U/ml)$ .  $G_b$  and  $I_b$  are the basal pre-injection level of glucose and insulin in the blood, respectively.  $D(t)$  Shows the amount of glucose absorbed in blood by food intake.  $n$  is the first order decay rate for insulin in plasma ( $1/min$ ) and  $h$  is the threshold value of glucose above which the pancreatic  $\beta$ -cells release insulin( $mg/dl$ ),  $\gamma$  is the rate of the pancreatic  $\beta$ -cells' release of insulin after the glucose injection with glucose concentration above the threshold ( $\frac{\mu U}{ml} \min^{-2} (\frac{mg}{dl})^{-1}$ ). The term  $\gamma[G(t)-h]^+$ , acts as an internal regulatory function that formulates the insulin secretion in the body, which does not exist in diabetic patients.  $u(t)$  is the input control signal or, in fact, the amount of insulin injected from the outside of the body ( $\mu U/ml$ ) [11].

Parameters  $p_1$ ,  $p_2$  and  $p_3$  are respectively, the maximum initial value of the glucose-insulin interaction curve ( $mg/dl$ ),  $p_2$  the amount of glucose reduction in tissue in each insulin unit ( $1/min$ ) and  $p_3$  glucose increase after insulin movement [14].

In this section, in order to simulate open circuit simulation of the body's blood glucose, the parameters of Table II which are parameters of the healthy person and diabetic patients' blood glucose, are used.

TABLE II  
PARAMETER VALUES [13]

	Normal	Patient 1	Patient 2	Patient 3
$p_1$	0.0317	0	0	0
$p_2$	0.0123	0.02	0.0072	0.0142
$p_3$	$4.92 \times 10^{-6}$	$5.3 \times 10^{-6}$	$2.16 \times 10^{-6}$	$9.94 \times 10^{-5}$
$\gamma$	0.0039	0.005	0.0038	0.0046
$n$	0.2659	0.3	0.2465	0.2814
$h$	79.0353	78	77.5783	82.9370
$G_b$	70	70	70	70
$I_b$	7	7	7	7
$G_0$	291.2	220	200	180
$I_0$	364.8	50	55	60

The simulation results of the plasma glucose concentration are shown in Fig. 9.

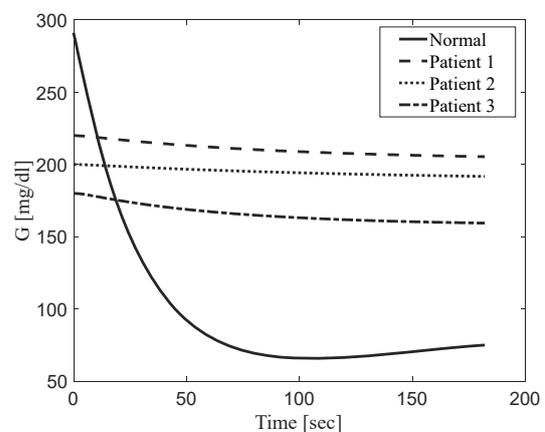


Fig. 9. Blood glucose concentration in healthy person and patients

#### IV. BERGMAN MODEL VERIFICATION

In this section, in order to illustrate the adaptation of the simulation results of the Bergman model with the data from patients and healthy person, MATLAB is used as it presented in Fig. 10. The proper adaptation of the graph which resulted from the numerical solution of Bergman's mathematical model with the clinical data shows the validity of the modeling process performed.

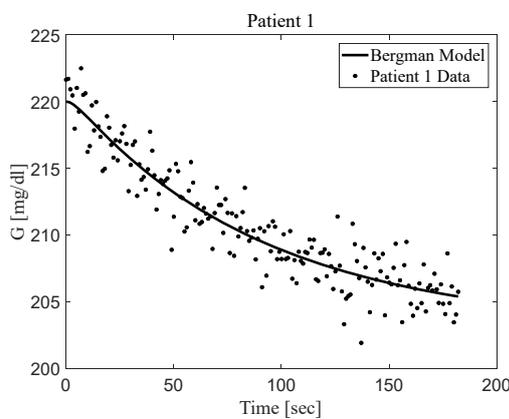


Fig. 10. Bergman model Verification of patient 1 data

Also, the modeling error analysis was performed based on Root Mean Square Error (RMSE). This criterion is as (4)

$$RMSE(x_1, x_2) = \sqrt{\frac{\sum_{i=1}^n (x_{1,i} - x_{2,i})^2}{n}} \quad (4)$$

The results of the error analysis in this modeling process and its validation are shown in Table III.

TABLE III  
RMSE RESULTS

Patient 3	Patient 2	Patient 1	Normal	
1.59141	1.59144	1.59143	$5.902 \times 10^{-2}$	RMSE

According to the results of Table III and Fig. 10, it is proved that in a closed loop system, the Bergman model is fully compatible with the available data of the patients and the healthy person.

#### V. FUZZY HIGH-ORDER SLIDING MODE CONTROLLER DESIGN

The main goal in diabetes treatment is to maintain normal blood glucose levels. As shown in Fig. 11, obtaining a control signal, which is the rate of insulin injection, is the most important issue in regulating blood glucose levels in the body. In this research, the diabetic patient's body model is considered as a nonlinear model, so a nonlinear controller is designed to create a control signal. According to the block diagram, Fig. 11 shows the rate of insulin injection as a control signal by a pump to a diabetic patient. The input of control algorithm is the desired level of injectable insulin to the blood and the output should also be the desired level of glucose adjusted by the control method. Also, the purpose of this research is the development of the control strategy that yields to produce an appropriate control signal for the injection pump not to improve the dynamic model of the pump. Therefore, the dynamical model of the injection pump is not considered in this work.

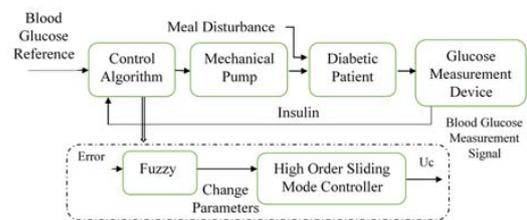


Fig. 11. Closed loop control system using FHOSMC

The system in the Bergman equation can be rewritten in the form of the space state as follows

$$\begin{cases} \dot{x}_1 = -p_1[x_1 - G_b] - x_1x_2 + D(t) \\ \dot{x}_2 = -p_2x_2 + p_3[x_3 - I_b] \\ \dot{x}_3 = -n[x_3 - I_b] + \gamma[x_1 - h]^+ t + u(t) \end{cases} \quad (5)$$

In (5), the trace error is defined as the difference between the concentration level of glucose and its base value in the blood of the diabetic patient in the form of relation (6):

$$e = G_b - G(t) = G_b - x_1 \quad (6)$$

For the system of order three according to the dynamical equation (5), after calculating the derivative of order three in the form of (7), the system equation is written as the conventional equation in the sliding mode control system.

$$x_1^{(3)} = \phi(x, t) - p_3x_1u(t) \quad (7)$$

The sliding variable is also designed as (8)

$$\sigma = \ddot{e} + c_1\dot{e} + c_0e \quad (8)$$

In (8), the values  $c_1, c_0$  are real-valued constants and are chosen to optimize the behavior of the system. In order to investigate the sliding mode, by deriving from (8), the sliding variable is obtained as (9):

$$\dot{\sigma} = \ddot{\ddot{e}} + c_1\ddot{\dot{e}} + c_0\ddot{e} \quad (9)$$

Also, by combining and simplifying the equations mentioned above, the sliding variable can be expressed as (10)

$$\dot{\sigma} = \psi(t) + p_3x_1u(t) \quad (10)$$

Which we have from (10)

$$\psi(t) = -\phi(x, t) + c_1\ddot{e} + c_0\dot{e} \quad (11)$$

In order to stabilize the sliding mode control system,  $\psi(t)$  must be reduced by a positive amount [11].

$$|\dot{\psi}(t)| \leq N \quad (12)$$

It is clear from (5), (6) and (7) that the sliding surface is zero, and in fact, the system dynamics is placed on a sliding mode, and thus, an appropriate control input can be design for (5). Given the dynamical system introduced in (5), the control function  $u(t)$  is obtained as (13) [11]:

$$u = -\alpha_1|S|^{\frac{1}{2}}\text{sign}(S) - \beta_1 \int \text{sign}(S)d\tau \quad (13)$$

$$\begin{aligned} \alpha_1 &= 1.25 \times 10^4 \sqrt{N} \\ \beta_1 &= 0.92 \times 10^4 N \end{aligned}$$

In the control structure of the high-order sliding mode, according to [11], the coefficients  $\alpha_1$  and  $\beta_1$  are considered as fixed numbers. For the exact adjustment of these coefficients, no proper solution has been found, and its values are considered mainly in terms of trial and error.

In this study, in order to achieve better control results and to reduce the disturbance and unwanted factors as well as to more precisely determine the amount of  $u$ , a fuzzy inference system to determine the coefficients  $\alpha_1$  and  $\beta_1$  have been used. In this fuzzy system, the input is error value and the derivative of the error. The error rate is the difference between the level of glucose in the body and the amount that is desired, and the desired amount of glucose is considered to be 70 approximately for a healthy person. After the fuzzy inference between the error values and the control parameter values, the output of the fuzzy system consists of the values of  $\alpha_1$  and  $\beta_1$ .

In the fuzzy section, the control input is the error between the glucose reference value and the instantaneous and derived error, and the output is the amount of insulin injected. To obtain the amount of insulin injected, a fuzzy inference system is used, which results in a more accurate calculation of the control coefficients  $\alpha_1$  and  $\beta_1$  values. Fig. 12 shows the input and output of the fuzzy block. In the model presented in [13], only one of the constant coefficients ( $k$ ) in the control signal of the fuzzy system is used, whereas in this study, the dual fuzzy control system is presented which both of the constant control signal coefficients  $\alpha_1$  and  $\beta_1$  is obtained simultaneously with the fuzzy inference method, and as a result, the blood glucose level is reached to desire point faster and more accurate.

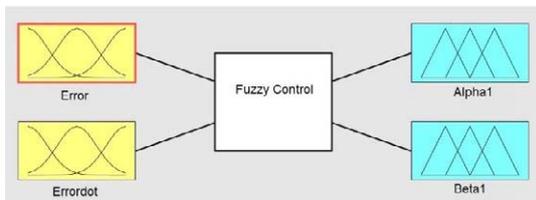


Fig. 12. Fuzzy block inputs and outputs

The fuzzy controller block changes the parameters of the control system in the limited range so that the stability of the closed-loop system is guaranteed.

## VI. SIMULATION RESULTS

In this section, a fuzzy high-order sliding mode controller and a high-order sliding mode controller are simulated in closed loop mode. This simulation was performed for a healthy and diabetic patient based on the parameter's value in Table II. Thus in order to observe the stability of this controller against disturbances, all simulations have been performed in both cases with and without disturbance.

### 1. Simulation without disturbance

In Figs. 13, 14 and 15, the controllers' performance on the body of a healthy person and the diabetic patient is given without consideration of disturbance. The following diagrams describe the responses of the high-order sliding mode controller with the HS label and the responses of the fuzzy high-order sliding mode controller with the FHS label.

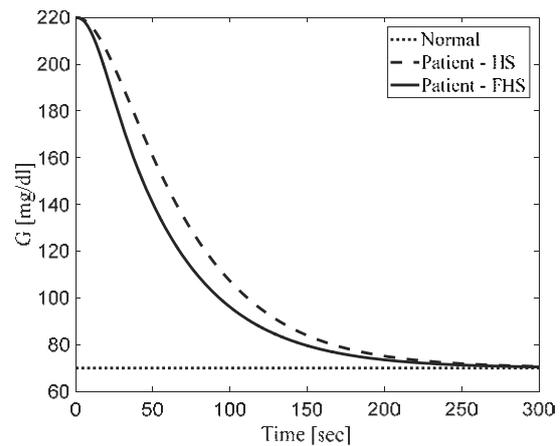


Fig. 13. Blood glucose level of a healthy and type 1 diabetic patient

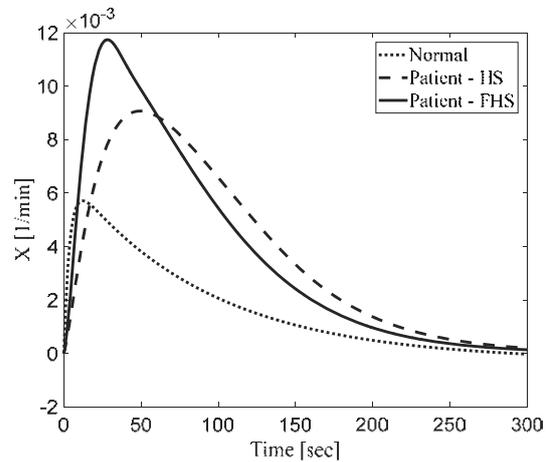


Fig. 14. Insulin effect on glucose disappearance of a healthy and type 1 diabetic patient

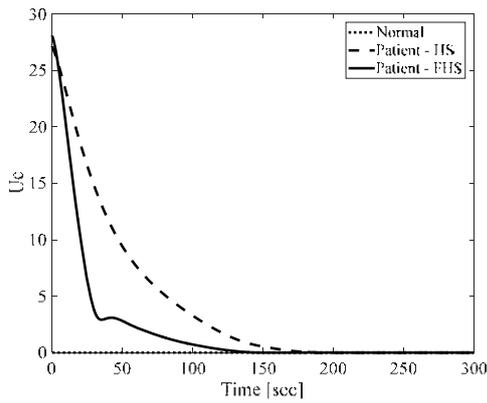


Fig. 15. Control signal of a healthy and type 1 diabetic patient

As shown in (13) and (14), the fuzzy high-order sliding mode controller is superior to the high-order sliding mode controller in terms of response time, the configuration of the system variables as well as control input.

2. FHOSMC performance and stability

In order to evaluate the performance of fuzzy high-order sliding mode controller and high-order sliding mode controller, the ISE and IAE errors have been used, as well as the steady-state error and the settling time of the closed-circuit system response. In Table IV, a comparison of the controllers' performance for the diabetic patient's physical parameters in the absence of disturbance is presented.

For this purpose, the criteria for ISE and IAE errors are used in the form of (14) and (15).

$$ISE = \int e(t)^2 dt \tag{14}$$

$$IAE = \int |e(t)| dt \tag{15}$$

TABLE IV  
CONTROLLER FUNCTION IN DIABETIC PATIENT WITHOUT DISTURBANCES

FHOSMC	HOSMC	Error in (s)
200	218.7	Settling time
0.01	0.01	Steady state error
811	850	ISE( $\times 10^3$ )
9.18	10.2	IAE( $\times 10^3$ )

To study the robustness of the designed control system and the effect of disturbance on the function of the controllers on the diabetic patient's body, the disturbance  $D(t) = 0.5 e^{-0.05t}$  has been applied to the controllers. In fact, the disturbance function  $D(t)$  is the amount of glucose mathematical model which is transferred to the body by eating food. In Figs. 16, 17 and 18, the fuzzy high-order sliding mode controller for a diabetic patient in the pre and post-disturbance action has been investigated. Whereas, the low impact of this disturbance against the designed controller and proper stability in contrast with unwanted factors and ultimately robustness of fuzzy high-order sliding mode structure is shown.

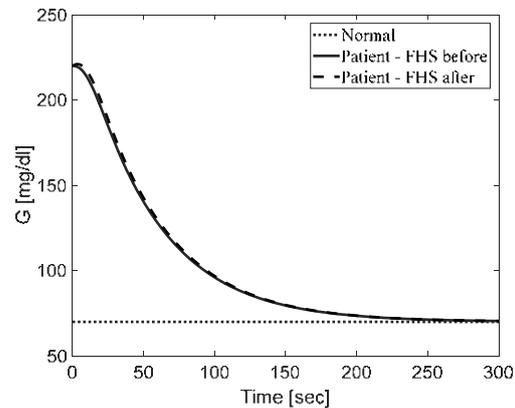


Fig. 16. Blood glucose level of a healthy and a diabetic patient pre and post disturbance

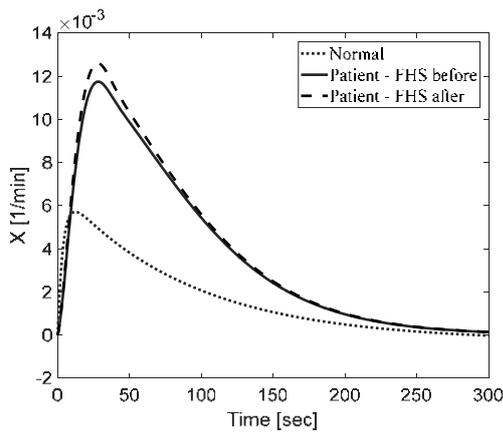


Fig. 17. Insulin effect on glucose disappearance of a healthy and type 1 diabetic patient pre and post disturbance

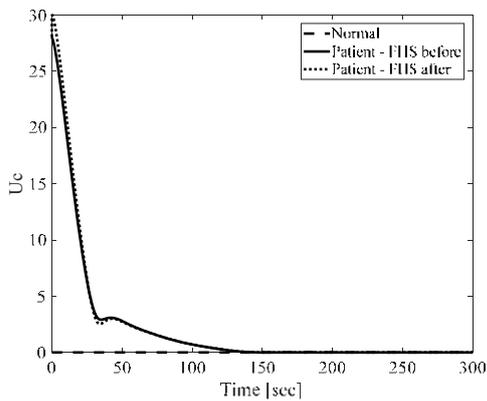


Fig. 18. Control signal of a healthy and type 1 diabetic patient pre and post disturbance

Table V shows the controllers' performance comparison for the diabetic patient's physical parameters in presence of the disturbance.

TABLE V  
CONTROLLER FUNCTION IN DIABETIC PATIENT WITH DISTURBANCES

FHOSMC	HOSMC	Error in (s)
201.4	220.9	Settling time
0.01	0.01	Steady state error
855	883	ISE( $\times 10^3$ )
9.5	10	IAE( $\times 10^3$ )

As the results presented in Tables IV and V show, the presence of disturbance does not have a significant effect on the performance of this controller, so we conclude that the designed fuzzy high-order sliding mode controller is resistant to disturbances and unwanted agents.

## VII. CONCLUSION

In this paper, Wolf's algorithm was used to calculate the time series of the Lyapunov exponents in order to analyze the blood glucose-insulin system's behavior in diabetic patients. These time series are samples taken from diabetic patients and healthy person, which indicates that the positivity of the Lyapunov exponents is the chaotic dynamics of the systems. Also, the power spectral density function method was used to study the type of behavior of these time series. The study, with both methods, ended with a single result that was chaotic in this system. Then, the Minimal Bergman model was used to model these time series. In order to confirm the modeling process, the results of the numerical solution of the Bergman model equations with the clinical data were compared, and their correlation and RMSE analysis criterion indicate that the model is compatible. In the following, a novel fuzzy high-order sliding mode controller was used to control the system. The simulation results of this controller with the high-order sliding mode controller designed in [11] were compared and the performance of the feedback system in different conditions Reviewed. Comparing the results of the proposed control systems, even in

the presence of disturbances, indicates the high performance of the fuzzy high-order sliding mode control system, as well as the robustness of the controller against disturbances. Thus, the responses of the fuzzy high-order sliding mode control system resulted in a reduction of about 10% at the settling time a reduction of 11% in steady state error compared to the high-order sliding mode controller. Therefore, the results of the control system indicate a high-speed fuzzy high-order sliding mode controller in order to close the blood glucose level to the optimum level in diabetic patients, so using this intelligent controller can be very efficient in artificial pancreas structure for diabetic patients Type I.

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