# An Adaptive Backstepping Based Nonlinear Controller for Patients with Type 1 Diabetes


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# Approval

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# Abstract

Automatic controllers for insulin infusion are used in artificial pancreas for treatment of diabetes type 1 patients. Controllers are designed based on some models of blood glucose-insulin system. A physiologically verified model that governs the characteristics of human blood glucose is Bergman's nonlinear model. Using this model we have designed an adaptive backstepping based nonlinear controller for diabetes type 1 patients. For controller glucose effectiveness factor of blood is treated as an unknown parameter and numerical values of controller gain and tuning function are selected to produce best possible results. A complete mathematical derivation of nonlinear controller is described and simulation results are discussed using MATLAB SIMULINK. Lyapunov stability theorems are used to analyze stability and convergence of blood glucose level to a desired concentration. Lyapunov theorems propose exponential stability of controlled glucose concentration. Simulation results also indicate faster convergence in tracking response and overshoot/undershoot characteristics as compared to some recently developed techniques in literature. In the end a simple backstepping based nonlinear controller is also proposed. Again its exponential stability is proved mathematically and shown in simulations also. Comparison of SIMULINK results with adaptive backstepping based controller is discussed in the last chapter.

Keywords: Artificial pancreas, diabetes controller, adaptive backstepping, Lyapunov stability.

# Dedication

I dedicate this thesis to my parents and teachers.

# Certificate of Originality

I hereby declare that this submission is my own work and to the best of my knowledge it contains no materials previously published or written by another person, nor material which to a substantial extent has been accepted for the award of any degree or diploma at NUST SEECS or at any other educational institute, except where due acknowledgement has been made in the thesis. Any contribution made to the research by others, with whom I have worked at NUST SEECS or elsewhere, is explicitly acknowledged in the thesis.

I also declare that the intellectual content of this thesis is the product of my own work, except for the assistance from others in the project's design and conception or in style, presentation and linguistics which has been acknowledged.

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# Acknowledgment

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# Chapter 1

# Preliminaries

## 1.1 Linear Systems

A linear system is one that satisfies properties of superposition and homogeneity. A general form of a linear system is

$$\begin{aligned} \dot{x} &= A(t)x + B(t)u \\ y &= C(t)x + D(t)u \end{aligned} \tag{1.1}$$

where "x" is the state vector, "y" is output and "u" is input. Matrices A, B, C and D depend on the model parameters.
**Superposition:** If u(t) is input of a system and y(t) is output and for two different inputs $u_1(t)$ & $u_2(t)$ outputs are $y_1(t)$ & $y_2(t)$ than system is said to hold superposition property if $u_1(t) + u_2(t) = y_1(t) + y_2(t)$.
**Homogeneity:** If y(t) is output of a system against an input u(t) and "$a$" is a scalar number than for homogeneity $au(t) = ay(t)$ should be satisfied.

## 1.2 Nonlinear Systems

Nonlinear systems do not posses superposition and homogeneity properties. In mathematical models of nonlinear systems there are nonlinear terms in state equations. An example of a nonlinear time invariant system $\dot{x} = f(x, u)$ is given below:

$$\begin{aligned} \dot{x_1} &= a_1x_1 + b_1x_1x_2 + c_1x_3 \\ \dot{x_2} &= a_2x_2 + b_2x_3^2 + c_3x_2x_3 \\ \dot{x_3} &= a_3x_1 + b_3x_2 + c_3x_3 \end{aligned} \tag{1.2}$$

In this model there are three nonlinear terms in first two equations i.e. $b_1x_1x_2, b_2x_3^2$ and $c_3x_2x_3$. Where coefficients $a_1, b_1, c_1, a_2, b_2, c_2, a_3, b_3$ and $c_3$ are real numbers.

## 1.3 Lyapunov Stability Theory

Information about energy of a system can be a useful to determine whether a system is stable or not. If the energy of a system is decreasing it is stable and if it is increasing then unstable. e.g. If a ball is dropped vertically from a height its total energy will be sum of potential and kinetic energy. After some time this ball will hit the ground and eventually become static with zero energy due to resistive forces acting against its motion. Therefore we can conclude that a ball dropping vertically from certain height is stable as its energy is decreasing. This concept was first introduced by a Russian mathematician Aleksandr Mikhailovich Lyapunov and hence theory was named after his name. Lyapunov stability theory describes stability of a system in terms of its energy i.e. if energy of a system is decreasing with time it is stable.
To determine whether energy of a system is decreasing or increasing we can simply write down energy function of a system e.g. as in a mechanical system sum of all the energies (kinetic and potential). This function is called a Lyapunov candidate function. After that we take time derivative of Lyapunov candidate function if the derivative comes out to be negative it means system is stable. In many problems we do not know the exact energy function of the system. In that case Lyapunov candidate function is not a perfect energy function but an energy like positive definite function in which all the state variables of system are included.

Another important point is that if derivative of candidate function cannot be proven negative it does not mean that system under consideration is unstable. It may be stable or unstable because sometimes a system is stable but we can not prove it mathematically due to different choice of Lyapunov candidate functions. Therefore by using Lypunov theory we can only prove that system is stable but can not say for sure that it is unstable. Because there may exist a different candidate function for which derivative comes out to be negative but we do not know it yet.
For a general three state system, given below;

$$\begin{aligned} \dot{x_1} &= f_1(x_1, x_2, x_3) \\ \dot{x_2} &= f_2(x_1, x_2, x_3) \\ \dot{x_3} &= f_3(x_1, x_2, x_3) \end{aligned} \tag{1.3}$$

We can define a Lypunov candidate function "V" such that it is a positive definite function with all three state variables included in it. Few examples of positive definite function for system 1.3 with three state variables are given below;

$$V = x_1^2 + x_2^2 + x_3^2 \tag{1.4}$$

$$V = x_1^2|x_2| + x_3^2 \tag{1.5}$$

$$V = |x_1| + |x_2| + \dot{x_3}^2 \tag{1.6}$$

Using lyapunov stability theory we can define three types of stable systems. i.e. stable, asymptotically stable and exponentially stable.

### 1.3.1 Stability

A system is said to be stable if it has a bounded output against a bounded input. In terms of Lypunov theory a system is stable if derivative of Lyapunov candidate is less or equal to zero.

### 1.3.2 Asymptotic Stability

A system is asymptotically stable if it has bounded output for a bounded input and it converges to origin with the passage of time. Mathematically a system can be proven asymptotically stable if time derivative of Lypunov function is negative definite.

### 1.3.3 Exponential Stability

An asymptotically stable system is said to be exponentially stable if it converges to origin with an exponential decay. According to Lyapunov theory, a system is said to be exponentially stable if for a positive definite Lyapunov candidate function V(x), the derivative $\dot{V}(x)$ is negative definite such that $\dot{V}(x) \leqslant -\alpha V(x)$.

### 1.3.4 Local and Global Stability

Locally stable systems are stable for a set of initial conditions but not stable for initial conditions that are outside the set. While globally stable systems are stable for all the possible input conditions. In other words we can say that for a locally stable system region of attraction is a limited set and system can converge to origin for the initial conditions within that set. A globally stable system has an unlimited set as region of attraction.
In terms of Lyapunov theory a system is globally stable if derivative $\dot{V}(x)$ is negative and V(x) is radially unbounded.

## 1.4 Backstepping

Backstepping is a technique in which stabilizing control for a nonlinear system (in strict feedback form) is designed in a recursive way where a system can be divided into subsystems and these subsystems can be stabilized by choosing appropriate virtual inputs [23]. Resulting control law obtained in such a way is robust for both matched and mismatched disturbances. A matched disturbance is one that appears in the same state in which input is present. While a mismatched is in a different state from input e.g. in blood a glucose input is treated as a mismatched disturbance because input to control glucose level is insulin, later it will clear in discussion of blood glucose model.
A four state model in strict feedback form is shown in eqn. 1.7. We can divide this system into four subsystems and stabilize each one separately, for this we have to take virtual inputs for each subsystem. e.g. For $\dot{x_1}$, $\dot{x_2}$ and $\dot{x_3}$ we can take $x_2$, $x_3$ and $x_4$ as virtual inputs and finally, control input "u" can be derived.

$$\begin{aligned} \dot{x_1} &= f_1(x_1) + g_1(x_1)x_2 \\ \dot{x_2} &= f_2(x_1, x_2) + g_2(x_1, x_2)x_3 \\ \dot{x_3} &= f_3(x_1, x_2, x_3) + g_3(x_1, x_2, x_3)x_4 \\ \dot{x_4} &= f_4(x_1, x_2, x_3, x_4) + g_4(x_1, x_2, x_3, x_4)u \end{aligned} \tag{1.7}$$

## 1.5 Adaptive Control

Adaptive control is a control technique useful when some system parameters are variable or uncertain. Because adaptive controller adapts to the new conditions if value of some parameter changes. e.g. In a rocket, airplane or helicopter flight quantity of fuel in the fuel tank is not a constant, it varies as the time of flight increases. Therefore to overcome the effect of variable fuel quantity adaptive controller is a suitable choice.

## 1.6 Robust Control

Robust controllers are used where we have uncertain parameters, matched or mismatched disturbances and modelling errors. This is a static technique in which effect of errors and uncertainties is canceled out by introducing a gain in controller which is larger than any possible uncertainty/disturbance. Hence robust controller does not adapts to the changes in parameters as in adaptive controller, it just has the ability to overcomes any uncertain situation. Another difference is that for robust controllers bounds of uncertainty/error/disturbance should be known which is not necessary for adaptive

controllers. e.g. In an aircraft flight suppose it is hit by some object (bird etc.) which disturbs the stability of aircraft. This is where robustness comes in handy to bring back that airplane to stability.

## 1.7 Matched and Mismatched Disturbance

A matched disturbance is one that, if represented in mathematical model of a system, appears in the same state equation in which control input is available. e.g. In a four state system model shown below a disturbance $d_3(t)$ is matched disturbance because of the presence of control input "u".

$$\begin{aligned} \dot{x_1} &= f_1(x_1) + g_1(x_1)x_2 + d_1(t) \\ \dot{x_2} &= f_2(x_1, x_2) + g_2(x_1, x_2)x_3 + d_2(t) \\ \dot{x_3} &= f_3(x_1, x_2, x_3) + g_3(x_1, x_2, x_3)x_4 \\ \dot{x_4} &= f_4(x_1, x_2, x_3, x_4) + g_4(x_1, x_2, x_3, x_4)u + d_3(t) \end{aligned} \tag{1.8}$$

A mismatched disturbance is one that is in the state equation in which there is no control input. e.g. In above model $d_1(t)$ and $d_2(t)$ are mismatched disturbances.

# Chapter 2

# Introduction

Diabetes is one of the most common diseases which results in deaths of millions of patients per year around the world. Diabetes is a widespread disease in the whole world with billions of dollars spent on its treatment on yearly basis. In year 2002 total medical expenses on treatment of diabetes in US were estimated to be $ 132 billion which exceeded to $ 245 billion by 2012 [7], [2]. Studies also indicate that number of patients worldwide may increase to 300 million by year 2025, this number was much less back in 1995 with 135 million patients [24]. Total diagnosed diabetes patients in US in year 2007 were 17.5 million with total medical expenditure of $ 174 billion and this number is increasing ever since [1]. Diabetes cases can be divided into two major etiopathogenetic categories. Diabetes mellitus type 1, traditionally termed as "juvenile diabetics", is a disease in which patient has high blood glucose level due to insulin deficiency. This lack of insulin is resulted by loss of insulin producing beta cells of the islets of langerhans in the pancreas, for which insulin therapy is necessary for affected individuals. Although it can occur at any age, it mostly occurs in childhood or adolescence. Type 2 diabetes is caused by two main factors (i) combination of resistance to insulin action (ii) inadequate insulin secretory response. It is uncommon under the age of 40 and number of cases increase with increase of age [3] & [9].
Diabetes if not controlled can result in life threatening consequences such as hyperglycemia with ketoacidosis or the non ketotic hyperosmolar syndrome. Hyperglycemia causes dysfunction and failure of eyes, kidneys, heart and blood vessels [3]. Therefore proper control of blood glucose in human body is of primary importance. This bleak situation has motivated many researchers to look for new methods and ways of improvement in treatment of diabetes.

Infusing insulin externally to overcome the lack of insulin in human body

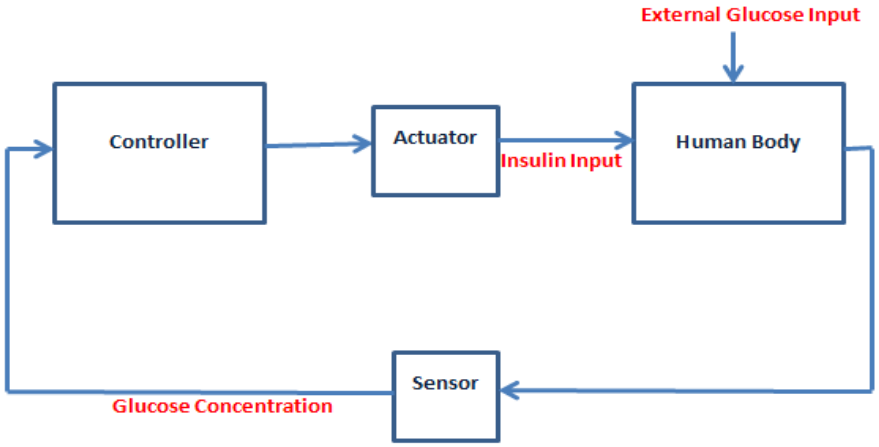


Figure 2.1: Closed Loop Control of Blood Glucose

is the most effective and commonly used method for treatment of type 1 diabetes patients. This infusion can be done by injecting insulin into body manually or automatically by using some controller. For patients who use insulin manually before sleeping or before fasting a very common condition observed during sleep is nocturnal hypoglycemia/hyperinsulinemia. By using overnight closed loop control episodes of nocturnal hypoglycemia can be reduced significantly [19], [20]. Therefore, it is preferred to use closed loop control during night and fasting conditions. During day time and normal conditions (without fasting) a good control sequence can also be used to control glucose concentrations. A simplified closed loop feedback system is shown in Fig. 1, which shows a sequence in 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 body through an actuator. A real time artificial pancreas is also shown in Fig. 2.2 and its application on human body is elaborated in Fig. 2.3.
The measure of effectiveness or quality of a controller to be used in an artificial pancreas can be studied by (i) convergence time to different glucose set points, overshoot/undershoot from set points & steady state error and by (ii) (a) OGTT (Oral Glucose Tolerance Test i.e. ingesting glucose by mouth) (b) IVGTT (Intravenous Glucose Tolerance Test i.e. injecting glucose into body) & (c) MMTT (Mixed-Meal Tolerance Test i.e. taking a dose of mixed meal by mouth). In all three tests (a, b & c) response of controller against an external glucose input is studied by frequently taking blood samples and checking insulin resistance over a period of time [9].


Figure 2.2: An Artificial Pancreas (Ref: discovermagazine.com)

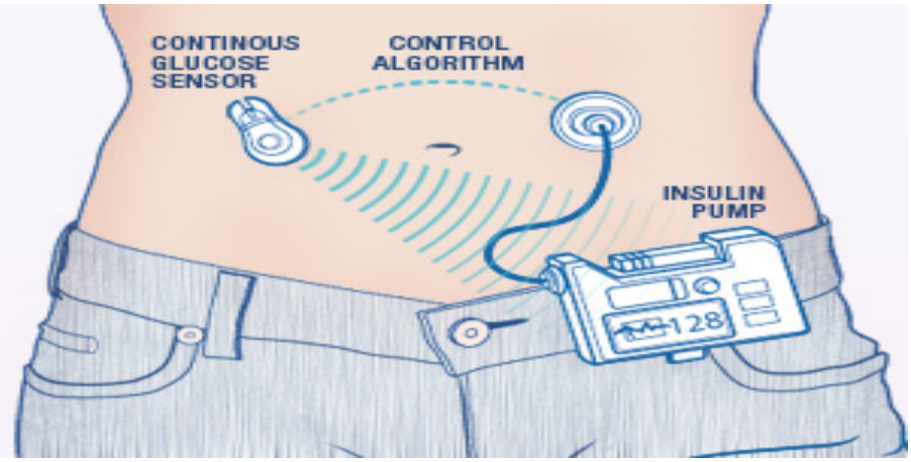


Figure 2.3: Artificial Pancreas Application (Ref: www.healthline.com)

In our research an adaptive backstepping based nonlinear controller is designed and its response to different set points, a sinusoidal glucose input disturbance and noise in measured glucose level is studied using MATLAB SIMULINK. Controller is derived mathematically using adaptive backstepping technique and its stability analysis is performed using Lyapunov stability theory. Comparison of proposed controller is made with some other control techniques and simulation results are also discussed in detail.

# Chapter 3

# Literature Review

For automatic control of blood glucose many control techniques and algorithms are available in literature. Many methods are introduced for continuous insulin therapy since early years of 1970s. These control techniques include PID controllers, PD controllers, model predictive controllers, linear quadratic regulators, fuzzy controllers and empirical model based algorithms. Both black box and grey box based model strategies are available in literature [27]. Which are discussed in detail below:

## 3.1 Continuous Time Linear Control Techniques

In the very start curve fitting was used as first bedside control technique as described in [8] by clemens et al. A look up table based control was proposed by Furler et al in which an input value is decided from a table against an output value [14]. Application of optimal control theory to diabetes mellitus patients was studied in [34]. A rule based control with adaptive basal therapy was introduced by Wang et al. [46] in which control algorithm is adaptive for several basal profiles. A more mathematically based control strategy is discussed in [43] & [10]. PI controller and an improved PID switching based strategy are available in [15] & [33]. PID controller is generally considered the best as it can be tuned to minimize steady state errors [40]. Proportional, integral and derivative gains in PID controller can be adjusted to get the most optimized result of a controller. Proportional gain contributes to the speed of the controller while derivative and integral gains are used to control the overshoot/undershoot and steady state errors respectively. Some authors prefer PD controllers with high derivative gain and omitting integral gain to avoid overdosing of insulin.

## 3.2 Discrete Time Linear Control Techniques

Along with continuous time glucose controllers is discrete time controllers can also be applied for insulin infusion. Discrete time PID control is described in [44] and a continuous extended version of the same controller is design by Dalla Man et al. In which simulation results are discussed but for real time applications it should be discretised [10]. Basal insulin injection volumes can be optimized on run to run basis e.g. by studying the required insulin basal values of the previous days in different times during a day, present basal values can be optimized. This idea was shared by Palrem et al. in 2008[35].

## 3.3 Robust Control Techniques

Controllers have been designed to compensate disturbances in glucose level. Feedforward-feedback control strategies are available which preprocesses the effect of disturbance before the disturbance occurs. Similarly uncertainties in model parameters can also be compensated. Some robust control strategies for diabetes are available, a robust tracking problem is described in [39], an application of robust control on linearized system is discussed in [38] & an optimal controller for ICU applications was designed by Chee at al. in [6].

Sliding mode controller with two degree of freedom was proposed by Garcia Gabin et al [16]. In every sliding mode controller there is effect of chattering associated with it,a reduced chattering option was proposed by Kaveh and Shtessel in [22].

## 3.4 Model Predictive Control Techniques

Model predictive control (MPC) is another control method included in the domain of optimized control. MPC is a feasible technique for both linear and nonlinear models with powerful computational solvers. Model predictive control predicts the model of the system with passage of time and gives control input accordingly to the system [36], [29], [30] & [31]. Both linear model predictive control (LMPC), nonlinear model predictive control (NMPC) techniques are available in literature. An LMPC algorithm on a black box model was designed by Parker et al. [36] & [37]. To simulate response on an artificial pancreas a more detailed model is used in [42] & [42]. Linear discrete MPC based on model of Dalla Man et al. [12] & [11] is discussed in [30] by Magni et al. Along with linear continuous and discrete control techniques, nonlinear model predictive control (NMPC) was also proposed by Magni et al. using complete nonlinear model of Dalla Man et al. NMPC

uses a more detailed model and a different objective function which requires requires more computational effort. Hovorka et al. presented an adaptive NMPC based on a nonlinear model in [18]. It was specifically designed for patients with fasting condition with self adaptation of control algorithm to some insulin sensitive parameters. Another condition during glucose level control is hypoglycemia which should be avoided while infusing insulin. To control hypoglycemia a feedforward-feedback control strategy is described in [33] & [32] by Marchetti et al. Both the effect of insulin infusion on glucose level and of a known disturbance on glucose level should be known in this controller.

## 3.5 Advanced PID Control Techniques

Advancements in PID performance have been made by adding fuzzy control techniques resulting in PID type fuzzy controllers. A combination of PID and fuzzy controller is discussed in [26] by C. Li. and R. Hu. An application of multimodel based approach using fuzzy-PI and genetic fuzzy-PI controllers on diabetes type 1 patients is studied in detail by T. Vinod Reddy and M. Goharimanesh in [45] & [17] respectively.
Application of Linear Quadratic regulator (LQR) and empirical model based algorithm has also been studied [4].

## 3.6 Nonlinear Control Techniques

For nonlinear systems there are many nonlinear control techniques available in literature. These nonlinear control design techniques have been discussed in detail by Hassan Khalil in [23] and by Slotine et al. [41]. Some advanced nonlinear techniques are higher order sliding mode control, passivity based control, backstepping and adaptive backstepping based control and lyapunov redesign based control.

# Chapter 4

# Glucose-Insulin Nonlinear Model

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 respectively as elaborated in Fig. 4.1. A simplified model of blood glucose regulation is shown in Fig. 4.2 also. Characteristics of glucose-insulin dynamics in human blood can be represented by a mathematical model. 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 nonlinear model for blood glucose-insulin system is described in equations (1)-(3). This model was derived from work of R. N. Bergman and often referred to as Bergman's minimal model of glucose-insulin dynamics [5]. It is a physiologically verified three state model with identifiable parameters which takes into account the effect of glucose effectiveness ($p_1$) in human body and delay in insulin action ($p_2$) due to remote compartment of insulin. $G$, $X$, $I$, $U$ and $G_{meal}$ are glucose concentration, insulin concentration (remote compartment), plasma insulin concentration, insulin input (insulin infusion rate) and external disturbance of glucose, which is generally a meal disturbance, respectively.

$$dG/dt = -p_1 G - X(G + G_b) + G_{meal}/V_1 \tag{4.1}$$

$$dX/dt = -p_2 X + p_3 I \tag{4.2}$$

$$dI/dt = -n(I + I_b) + U/V_1 \tag{4.3}$$

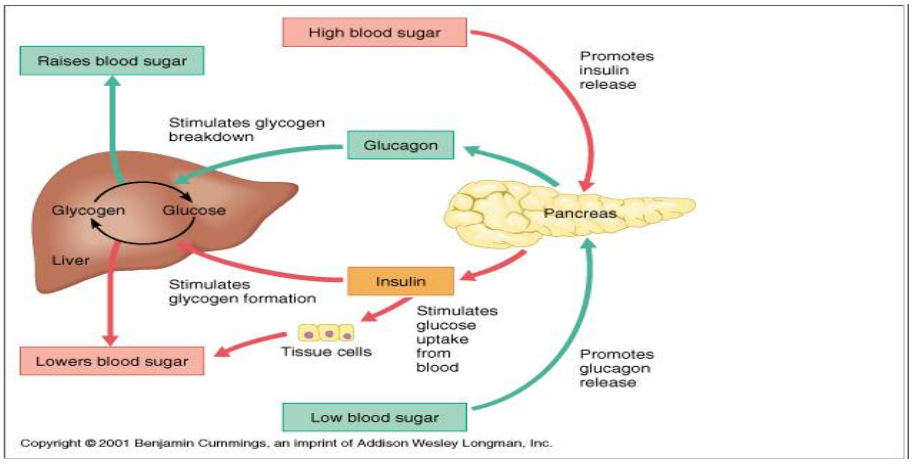


Figure 4.1: Glucose Regulation in Human Body (Ref: www.emaze.com)

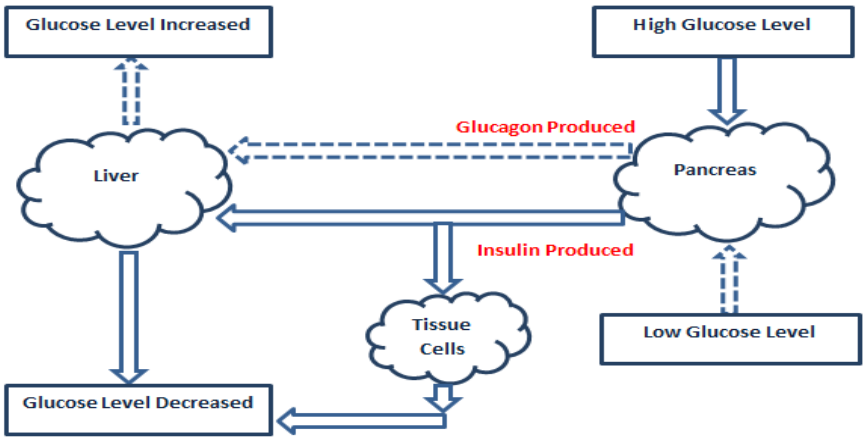


Figure 4.2: Model for Glucose Regulation

Parameters described in above model and their values is described in Table 4.1 To study comparison of results with some other controllers, parametric values are chosen exactly same as in [45] & [17].

Table 4.1: Parameters & Values

| Sr. no. | Parameter | Parameters Description | Values |
|---|---|---|---|
| 1 | $(G_b)$ | Basal Plasma Glucose | 4.5 mMol $L^{-1}$ |
| 2 | $(G_{meal})$ | External Glucose Input | 5.54 mMol $L^{-1}min^{-1}$ |
| 3 | $(p_1)$ | Glucose Effectiveness Factor | 0 $min^{-1}$ |
| 4 | $(V_1)$ | Insulin Distribution Volume | 12 L |
| 5 | $(p_2)$ | Delay in Insulin Action | 0.025 $min^{-1}$ |
| 6 | $(I_b)$ | Basal Plasma Insulin | 4.5 mU $L^{-1}$ |
| 7 | (n) | Fractional Disappearance Rate of Insulin | 5/54 $min^{-1}$ |
| 8 | $(p_3)$ | Patient Parameter | 0.000013 mU $L^{-1}min^{-2}$ |

## 4.1 Problem Statement

Current problems for designing artificial pancreas are continuous glucose measurement, controlling external glucose disturbances and effect of routine activity on glucose levels. Therefore improvements in sensors, modeling and control strategies are required. Here we shall try to improve the control algorithm for artificial pancreas. As discussed earlier actual model of glucose-insulin system is nonlinear, therefore, a nonlinear controller can be designed to achieve global stability instead of using linear techniques. The decision of nonlinear technique to be applied, largely depends on nonlinear model under consideration. Therefore first we have to analyze our three state model carefully.
For simplicity state variable $G$, $X$ and $I$ in equations (1)-(3) are replaced with $x_1$, $x_2$ & $x_3$ and the terms $G_{meal}/V_1$ & $U/V_1$ are replaced with $d(t)$ & $u$ respectively. Now model can be rewritten as:

$$\dot{x_1} = -p_1 x_1 - x_2(x_1 + G_b) + d(t) \tag{4.4}$$

$$\dot{x_2} = -p_2 x_2 + p_3 x_3 \tag{4.5}$$

$$\dot{x_3} = -n(x_3 + I_b) + u \tag{4.6}$$

Equations (4)-(6) describe a model of three states where in equation (4) we have a nonlinear term $x_2(x_1 + G_b)$ and a mismatched disturbance $d(t)$. Further, to study tracking response of controller, we have to introduce a set point variable $x_s$. A variable $z_1$ is chosen such that as $z_1$ approaches zero, $x_1$ approaches $x_d$ i.e.

$$z_1 = x_1 - x_d \tag{4.7}$$

Where $x_d$ is a set point for desired glucose level. Putting value of $x_1$ from equation (7) in our model with new variables, we have:

$$\dot{z_1} = -p_1(z_1 + x_d) - x_2(z_1 + x_d + G_b) + d(t) - \dot{x_d} \tag{4.8}$$

$$\dot{x_2} = -p_2 x_2 + p_3 x_3 \tag{4.9}$$

$$\dot{x_3} = -n(x_3 + I_b) + u \tag{4.10}$$

This form of model implies that the proposed controller should have the ability to track the set points in the presence of nonlinearities and mismatched disturbances in the system.

# Chapter 5

# Nonlinear Controller Design

## 5.1 Backstepping Based nonlinear controller

### 5.1.1 Introduction

Backstepping technique is a suitable choice for systems of this type if resulting controller meets our requirements [23]. Backstepping utilizes concept of virtual inputs.

### 5.1.2 Mathematical Derivation

**STEP I** First of all we take $x_2$ as virtual input for eqn. 5.1 further $x_2$ can be replaced with a function $\alpha_1$ which itself is a function of $z_1$ such that
First of all we take $x_2$ as virtual input for eqn. 5.1 further $x_2$ can be replaced with a function $\alpha_1$ which itself is a function of $z_1$ such that

$$z_2 = x_2 - \alpha_1 \tag{5.1}$$

Now, We can rewrite $\dot{z_1}$ as

$$\begin{aligned} \dot{z_1} &= -p_1(z_1 + x_d) - x_2(z_1 + x_d + G_b) + d(t) - \dot{x_d} \\ \dot{z_1} &= -p_1(z_1 + x_d) - (z_2 + \alpha_1)(z_1 + x_d + G_b) + d(t) - \dot{x_d} \\ \dot{z_1} &= -p_1 z_1 - p_1 x_d - z_1 z_2 - x_d z_2 - \alpha_1 z_1 - \alpha_1 x_d \\ & -G_b z_2 - G_b \alpha_1 + d(t) - \dot{x_d} \end{aligned} \tag{5.2}$$

Exact function $\alpha_1$ can be drawn using Lyapunov Stability Analysis.

$$V_1 = 1/2{z_1}^2 \tag{5.3}$$

$$\dot{V_1} = z_1 \dot{z_1} \tag{5.4}$$

Using eqn. 5.1 and taking following value of $\alpha_1$, $\dot{V_1}$ is shown in eqn. 5.19

$$\alpha_1 = (-p_1 x_d - \dot{x_d} + d(t)) * 1/(z_1 + x_d + G_b) \tag{5.5}$$

$\dot{V}$ takes following form(with $c_1 \geq 0$)

$$\dot{V_1} = -p_1 {z_1}^2 - (z_1 + x_d + G_b) z_1 z_2 \tag{5.6}$$

**STEP II** For eqn. 4.6 we can take $x_3$ as virtual input and replace it with $\alpha_2$ where $\alpha_2$ is a function of $z_1$ and $z_2$ such that

$$z_3 = x_3 - \alpha_2 \tag{5.7}$$

Now, eqn.s for $\dot{z_2}$ and $\dot{z_3}$ can be written as:
From eqn. 5.1 & 5.20 we can write

$$\begin{aligned} \dot{z_2} &= \dot{x_2} - \dot{\alpha_1} \\ \dot{z_2} &= -p_2 x_2 + p_3 x_3 - \dot{\alpha_1} \\ \dot{z_2} &= -p_2(z_2 + \alpha_1) + p_3(z_3 + \alpha_2) - \dot{\alpha_1} \end{aligned} \tag{5.8}$$

Now another Lyapunov candidate which includes both $Z_1$ and $z_2$ is

$$V_2 = V_1 + 1/2{z_2}^2 \tag{5.9}$$

Taking derivative w.r.t. time yields

$$\dot{V_2} = -p_1 {z_1}^2 - (z_1 + x_d + G_b) z_1 z_2 + z_2 \dot{z_2} \tag{5.10}$$

Putting $\dot{z_2}$ from eqn. 5.21 and following value of $\alpha_2$, $\dot{V_2}$ is shown in eqn. 5.25

$$\alpha_2 = 1/p_3[+p_2 \alpha_1 + \dot{\alpha_1} + (z_1 + x_d + G_b) z_1] \tag{5.11}$$

$\dot{V_2}$ comes out to be($c_2 \geq 0$)

$$\dot{V_2} = -p_1 {z_1}^2 - p_2 {z_2}^2 + p_3 z_2 z_3 \tag{5.12}$$

**STEP III** Again from eqn. 5.1 & 5.20 we can write

$$\begin{aligned} \dot{z_3} &= \dot{x_3} - \dot{\alpha_2} \\ \dot{z_3} &= -n x_3 - n I_b + u - \dot{\alpha_2} \\ \dot{z_3} &= -n(z_3 + \alpha_2) - n I_b + u - \dot{\alpha_2} \end{aligned} \tag{5.13}$$

Now we take one final Lyapunov Candidate which includes dynamics of all three states $z_1$, $z_2$ and $z_3$.

$$\begin{aligned} V_3 &= V_2 + 1/2{z_3}^2 \\ \dot{V_3} &= \dot{V_2} + z_3 \dot{z_3} \\ \dot{V_3} &= -p_1 {z_1}^2 - p_2 {z_2}^2 + p_3 z_2 z_3 \\ &+ z_3(-n z_3 - n\alpha_2 - n I_b + u - \dot{\alpha_2}) \end{aligned} \tag{5.14}$$

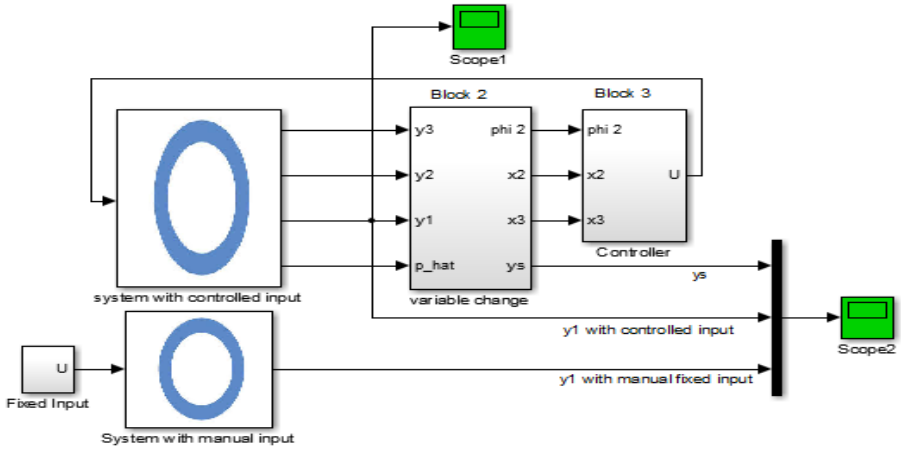


Figure 5.1: MATLAB SIMULINK Model

If we take

$$u = -p_3 z_2 + n\alpha_2 + nI_b + \dot{\alpha_2} \tag{5.15}$$

we have negative definite $\dot{V_3}$ which is

$$\dot{V_3} = -p_1 z_1 - p_2 {z_2}^2 - n{z_3}^2 \tag{5.16}$$

Negative definite derivative of Lyapunov candidate shows for input function given in eqn. 5.28 will be stable and exponentially converging to origin or the desired set point.

### 5.1.3 Simulation Results

Response of the proposed backstepping based controller can be studied in MATLAB SIMULINK using ODE45 solver. First of all analysis of performance is done at four different set points changing after regular time intervals. In simulations, a saturation function is used at controller output to limit infusion of insulin to a certain value which is 180 mU$L^{-1}min^{-1}$. Initial conditions of variables $x_1$, $x_2$ and $x_3$ are set to zero. Model implemented in SIMULINK is shown in Fig. 3. System with original variables is present in circled blocks, in block 2 change of variables is performed and controller is designed in block 3.

Using proposed controller for setpoints tracking, a graphical representation of system response can be seen in Fig. 4. It is clear how proposed controller keeps tracking four different glucose concentrations (4, 6, 8 & 10 mMol

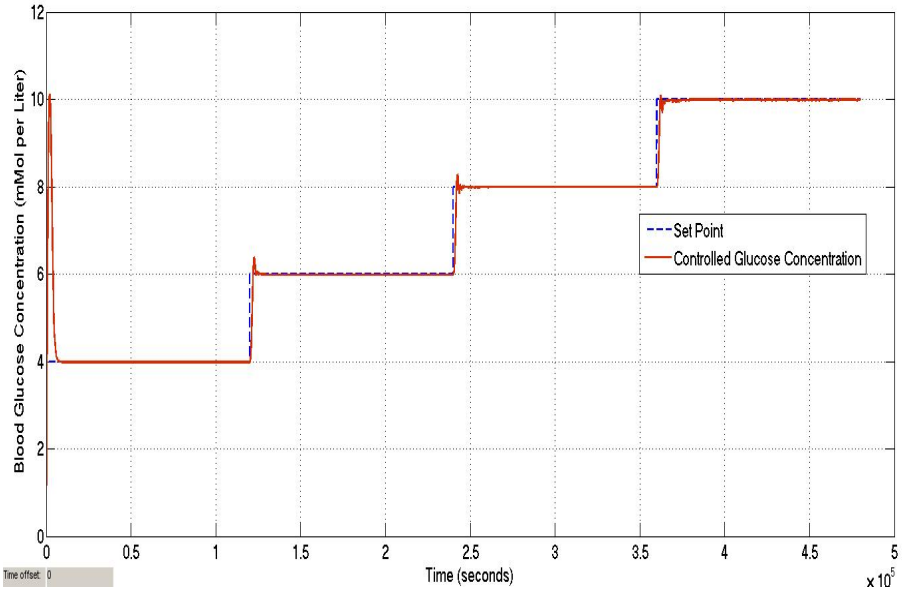


Figure 5.2: Setpoints Tracking with Backstepping Controller

per liter). Before convergence of glucose level to desired glucose concentrations, we can observe overshoots for all four setpoints. Maximum overshoot is observed when following first setpoint which is 6 mMol per liter. Longest convergence time also occurs at first setpoint tracking with 167 minutes (or approx. $1 * 10^4$ seconds) which is less for tracking other three concentration levels. This long convergence time is related to a delay between a time of glucose concentration measurement and a beginning of an action of insulin that is infused in response of a measured glucose concentration. However maximum time required to reach an acceptable range of glucose concentrations (rise time of controller) is 20 minutes for tracking of last setpoint 10 mMol per liter.

Any change in blood glucose level can be taken as a disturbance which is generally a meal disturbance. If a meal disturbance ($G_{meal}$) is introduced (as in OGTT or MMTT) which is less than 0.72 mMol $L^{-1}min^{-1}$, adaptive backstepping controller shows robustness against this external disturbance. When a sinusoidal meal disturbance is given to our system as shown in Fig. 5, variations in controlled blood glucose level can be seen in Fig. 6. It is clear how a disturbance in blood glucose results in variation from desired concentration but eventually it returns to the given setpoint. Now, practically blood glucose level is measured, frequently after small time intervals, with a sensor. Which means we may have a situation when there is a noise

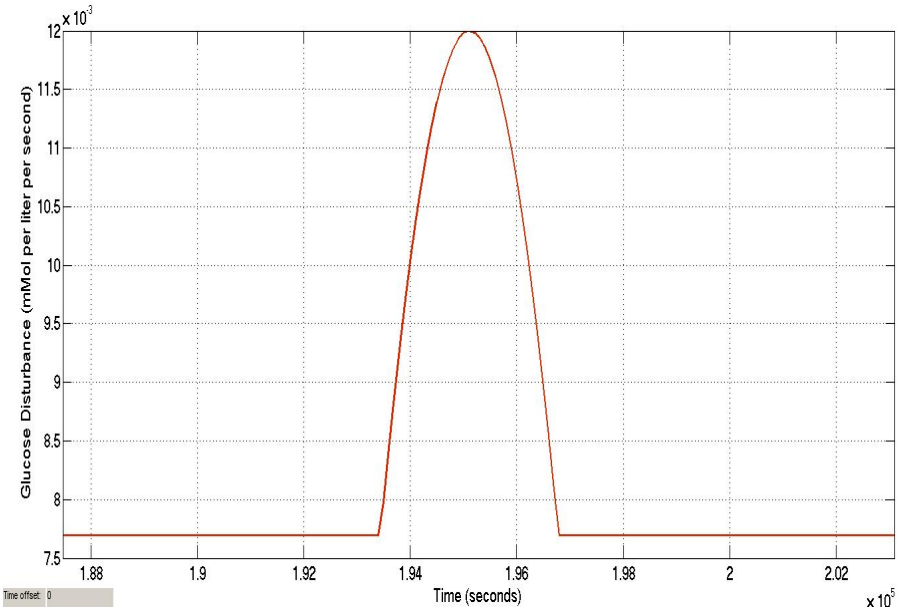


Figure 5.3: Glucose Disturbance Input ($G_{meal}/V_1$)

in measured glucose level. Under these circumstances simulation results of proposed controller are shown in Fig. 7 & Fig. 8. Where maximum noise is 0.72 mMol with a sampling time of 100 seconds.

### 5.1.4 Conclusion

Backstepping based controller can be used for insulin therapy of diabetes patients as glucose-insulin system is exponentially stable with controlled input.

## 5.2 Adaptive Backstepping based Nonlinear Controller

### 5.2.1 Introduction

An adaptive backstepping based controller can also be designed by adding adaptivity to backstepping based controller. Resulting control law will be adaptive for variable parameters of model and robust against matched and mismatched disturbances. A practically variable parameter is glucose effective factor ($p_1$) therefore we take $p_1$ as an unknown parameter while designing adaptive backstepping controller. A detailed mathematical derivation of

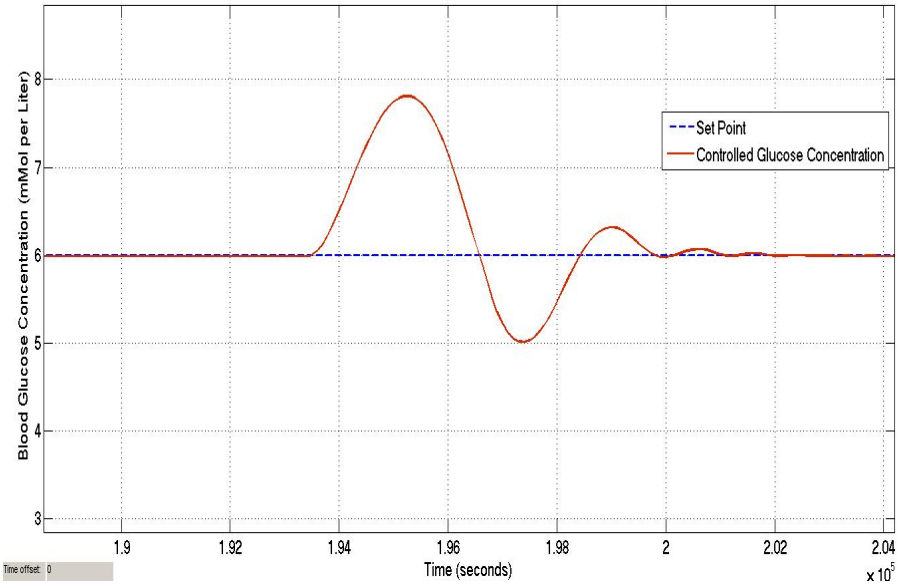


Figure 5.4: Response to Sinusoidal Disturbance of Backstepping Controller

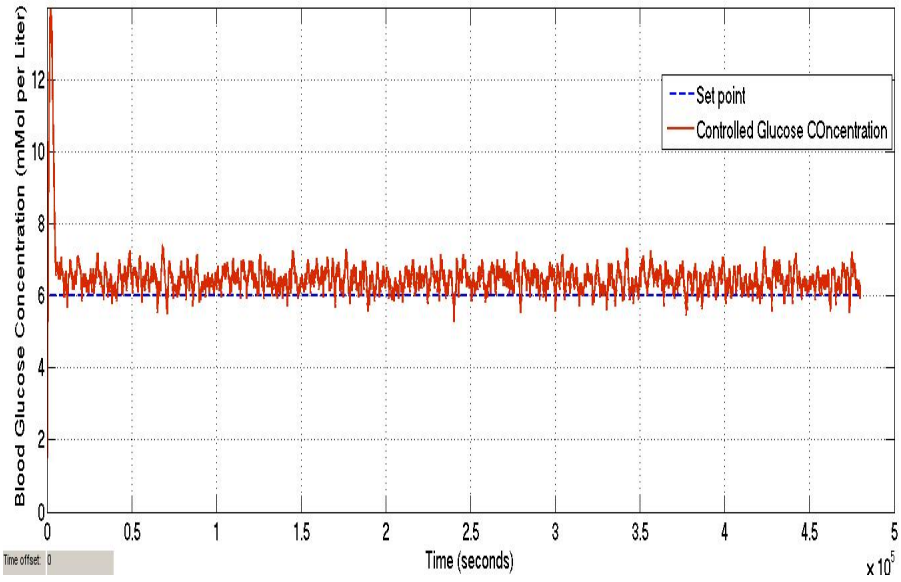


Figure 5.5: Response of Backstepping Controller Subjected to Noise

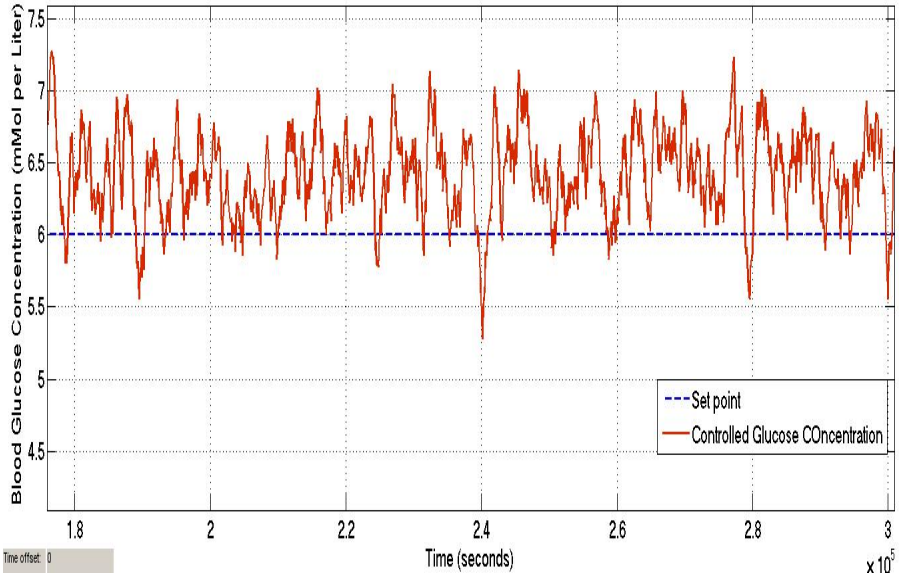


Figure 5.6: Response of Backstepping Controller Subjected to Noise

adaptive backstepping based controller is given below.

### 5.2.2 Mathematical Derivation

**STEP I**

First of all to make our controller adaptive, we take glucose effectiveness factor ($p_1$) as an unknown parameter. Using adaptive algorithm [25], [21], the estimated term $\dot{\hat{p}}_1$ for unknown parameter $p_1$ can be obtained in following three steps:

$$\begin{aligned} \omega_1 &= -x_1 \\ \tau_1 &= -z_1 x_1 \\ \dot{\hat{p}}_1 &= -z_1 x_1 \gamma \end{aligned} \tag{5.17}$$

where parameter $\omega_1$ is a function of the states directly affected by $p_1$, $\tau_1$ is tuning factor and $\gamma$ is a positive number.
If difference of estimated and actual value of $p_1$ is $\tilde{p_1}$, we can write

$$\tilde{p_1} = p_1 - \hat{p_1} \tag{5.18}$$

& its time derivative is

$$\dot{\tilde{p}}_1 = -\dot{\hat{p}}_1 \tag{5.19}$$

where $\dot{p_1} = 0$.
Now, in equation (8) we can take $x_2$ as a virtual input and apply an input $\phi_1$, which is a function of variable $x_1$, such that their difference $z_2$ can be written as:

$$z_2 = x_2 - \phi_1 \tag{5.20}$$

Putting this value of $z_2$ in equation (8), we have

$$\dot{z_1} = -p_1 z_1 - p_1 x_d - (z_2 + \phi_1)(z_1 + x_d + G_b) + d(t) - \dot{x_d} \tag{5.21}$$

or

$$\begin{aligned} \dot{x_1} = -p_1 z_1 - p_1 x_d - z_1 z_2 - x_d z_2 - \phi_1 z_1 - \phi_1 x_d \\ -G_b z_2 - G_b \phi_1 + d(t) - \dot{x_d} \end{aligned} \tag{5.22}$$

To determine $\phi_1$ in terms of state variables, we choose a positive definite Lyapunov candidate function $V_1$ such that effects of state $z_1$ and the error in estimated value of $p_1$ ($\tilde{p_1}$) are included in it.

$$V_1 = \frac{1}{2}{z_1}^2 + \frac{1}{2\gamma}{\tilde{p_1}}^2 \tag{5.23}$$

Taking its time derivative, we have

$$\dot{V_1} = z_1 \dot{z_1} + \frac{1}{\gamma}\tilde{p_1}\dot{\tilde{p}_1} \tag{5.24}$$

Putting values of $\tilde{p_1}$, $\dot{\tilde{p}_1}$ & $\dot{z_1}$ from equations (12), (13) and (16) respectively, in above equation (18), we have

$$\begin{aligned} \dot{V_1} = z_1(-p_1 z_1 - p_1 x_d - z_1 z_2 - x_d z_2 - \phi_1 z_1 - \phi_1 x_d \\ -G_b z_2 - G_b \phi_1 + d(t) - \dot{x_d}) - \frac{1}{\gamma}(p_1 - \hat{p_1})\dot{\hat{p}_1} \end{aligned} \tag{5.25}$$

In simplified form we can write equation (19) as:

$$\begin{aligned} \dot{V_1} = -z_1^2 z_2 - x_d z_1 z_2 - G_b z_1 z_2 - \hat{p_1} x_1 z_1 - z_1(\dot{x_d} - d(t) \\ +\phi_1 z_1 + \phi_1 x_d + \phi_1 G_b)) \\ \dot{V_1} = -(z_1 + x_d + G_b) z_1 z_2 - \hat{p_1} x_1 z_1 - z_1(\dot{x_d} - d(t) \\ +\phi_1(z_1 + x_d + G_b)) \end{aligned} \tag{5.26}$$

Now, taking following value of $\phi_1$

$$\phi_1 = (c_1 z_1 - \hat{p_1} x_1 - \dot{x_d} + d(t)) * \frac{1}{z_1 + x_d + G_b}, \tag{5.27}$$

equation (20) takes the form

$$\dot{V_1} = -c_1 z_1^2 - (z_1 + x_d + G_b) z_1 z_2 \tag{5.28}$$

**STEP II**

In equation (9) we take $x_3$ as a virtual input and apply an input $\phi_2$ in place of $x_3$, the difference between these two can be denoted by a variable $z_3$ such that

$$z_3 = x_3 - \phi_2 \tag{5.29}$$

A similar equation is (14) from which we can determine $\dot{z_2}$. Therefore by taking derivative of equation (14) and expanding it using equation (9) & (23), we have

$$\begin{aligned} \dot{z_2} &= \dot{x_2} - \dot{\phi_1} \\ \dot{z_2} &= -p_2(z_2 + \phi_1) + p_3(z_3 + \phi_2) - \dot{\phi_1} \\ \dot{x_2} &= -p_2 z_2 - p_2\phi_1 + p_3 z_3 + p_3\phi_2 - \dot{\phi_1} \end{aligned} \tag{5.30}$$

Now, we take an accumulative Lyapunov candidate function $V_2$, such that dynamics of $z_1$ & $z_2$ are included in it.

$$V_2 = V_1 + \frac{1}{2}{z_2}^2 \tag{5.31}$$

Taking derivative of $V_2$ and substituting values of $\dot{V_1}$ and $\dot{z_2}$ from equations (22) & (24), we have

$$\begin{aligned} \dot{V_2} &= \dot{V_1} + z_2\dot{z_2} \\ \dot{V_2} &= -c_1 z_1^2 - (z_1 + x_d + G_b) z_1 z_2 + z_2(-p_2 z_2 \\ &\qquad -p_2\phi_1 + p_3 z_3 + p_3\phi_2 - \dot{\phi_1}) \end{aligned} \tag{5.32}$$

or

$$\begin{aligned} \dot{V_2} = -c_1 z_1^2 - p_2 z_2^2 + p_3 z_2 z_3 - z_2((z_1 + x_d + G_b) z_1 \\ +p_2\phi_1 - p_3\phi_2 + \dot{\phi_1}) \end{aligned} \tag{5.33}$$

Now choosing

$$\phi_2 = \frac{1}{p_3}[(z_1 + x_d + G_b) z_1 + p_2\phi_1 + \dot{\phi_1}] \tag{5.34}$$

$\dot{V_2}$ takes the from

$$\dot{V_2} = -c_1 z_1^2 - p_2 z_2^2 + p_3 z_2 z_3 \tag{5.35}$$

**STEP III**

Taking time derivative of equation (23) and expanding it using equation (10), we have

$$\begin{aligned} \dot{z_3} &= \dot{x_3} - \dot{\phi_2} \\ \dot{z_3} &= -n(z_3 + \phi_2) - nI_b + u - \dot{\phi_2} \end{aligned} \tag{5.36}$$

Now another accumulative positive definite Lyapunov candidate function for all three states $z_1$, $z_2$ and $z_3$ is $V_3$.

$$V_3 = V_2 + \frac{1}{2}{z_3}^2 \tag{5.37}$$

Taking derivative of $V_3$ and putting values from equations (29) & (30), we have

$$\begin{aligned} \dot{V_3} &= \dot{V_2} + z_3\dot{z_3} \\ \dot{V_3} &= -c_1z_1^2 - p_2z_2^2 + p_3z_2z_3 + z_3(-n(z_3+\phi_2) - nI_b \\ &\qquad +u - \dot{\phi_2}) \\ \dot{V_3} &= -c_1z_1^2 - p_2z_2^2 - nz_3^2 + z_3(p_3z_2 - n\phi_2 - nI_b + u \\ &\qquad -\dot{\phi_2}) \end{aligned} \tag{5.38}$$

Here controlled input $u$ is derived such that derivative of accumulative Lyapunov function $V_3$ is negative definite. Clearly if we use following value of control input in equation (32),

$$u = -p_3z_2 + n\phi_2 + nI_b + \dot{\phi_2} \tag{5.39}$$

$\dot{V_3}$ becomes

$$\dot{V_3} = -c_1z_1^2 - p_2z_2^2 - nz_3^2, \tag{5.40}$$

which is clearly less than zero. It means with derived control input $u$, the derivative of positive definite Lyapunov function is negative definite. Therefore system modelled with states $z_1$, $z_2$ & $z_3$ is globally exponentially stable [28], [13]. We infer from this result that by using adaptive backstepping controller, for any initial conditions, state variables of system $z_1$, $z_2$, $z_3$ & $\tilde{p_1}$ (error in estimated parameter), all converge to zero exponentially.
Now, from equations (7) & (12) we see that as $z_1$ approaches zero, $x_1$(glucose concentration in blood) approaches $x_d$(set point) and as $\tilde{p_1}$ approaches zero, $\hat{p_1}$ approaches $p_1$ i.e. difference in estimated and actual value of $p_1$ becomes zero. It means when controlled input with adaptive backstepping controller is given to our system, glucose level will reach set points which is exactly what we were trying to achieve.

### 5.2.3 Simulation Results

Response of adaptive backstepping based controller can also be studied in MATLAB SIMULINK. In simulations, values of saturation function, $\gamma$ (a parameter used with tuning function in section IV) and controller gain $c_1$ are

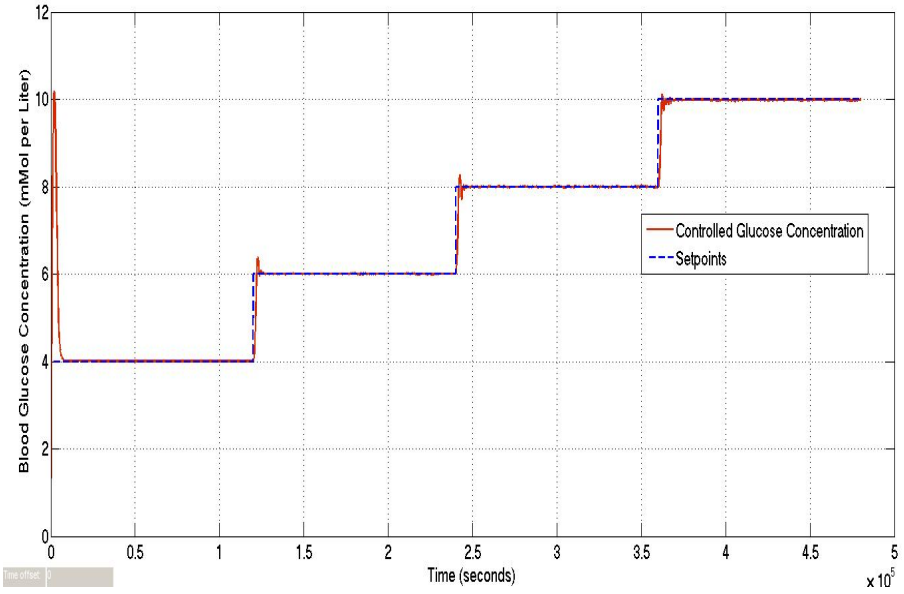


Figure 5.7: Setpoints Tracking with Adaptive Backstepping Controller

chosen as 180 mU$L^{-1}min^{-1}$, 0.005 and 1 respectively and again initial conditions of variables $x_1$, $x_2$ and $x_3$ are set to zero. In adaptive backstepping we can achieve as good results as simple backstepping for tracking, disturbance rejection and noisy conditions. An advantage is adaptivity of backstepping controller to variable parameters. Simulation results for tracking of setpoints, disturbance rejection and response to noise can be seen in Fig 11, 12 & 13 respectively. Disturbance input ($g_{meal}$) is sinusoidal and maximum value of noise is taken as 0.012 mMol.

Now, to compare results of proposed controller with some other controllers in literature, we take new set points (80, 95 , 115 & 95 same as in [45] & [17]). A combined graphical representation of set points $y_s$ (blue dash line) given to controller, system response with a manual fixed input (green dash-dot line) and response of glucose-insulin system with adaptive backstepping controller (red continuous line) is shown in Fig. 9. For simulation of manual infusion results, different insulin infusion rates ($u$) are selected for all four set points such that at steady state desired glucose concentrations are achieved. From this graph we can see how quickly convergence is achieved using adaptive backstepping controller as compared to manual infusion. Longest convergence time and maximum overshoot are observed at first setpoint (80) tracking which are 335 minutes (or $2 * 10^4$ seconds) and 6.5 mMol respectively.

Table 5.1 gives a comparison of adaptive backstepping controller with multi-

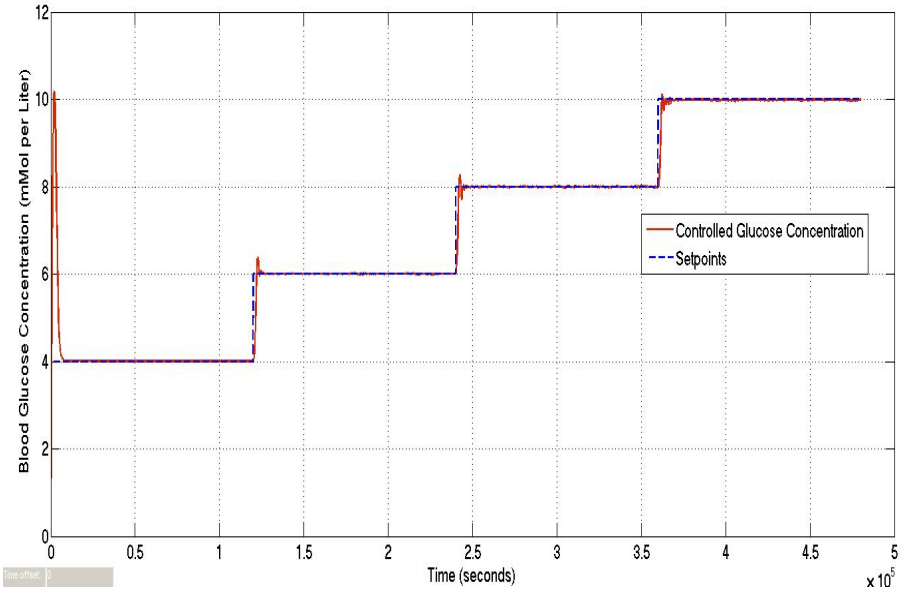


Figure 5.8: Response to Sinusoidal Disturbance of Adaptive Backstepping Controller

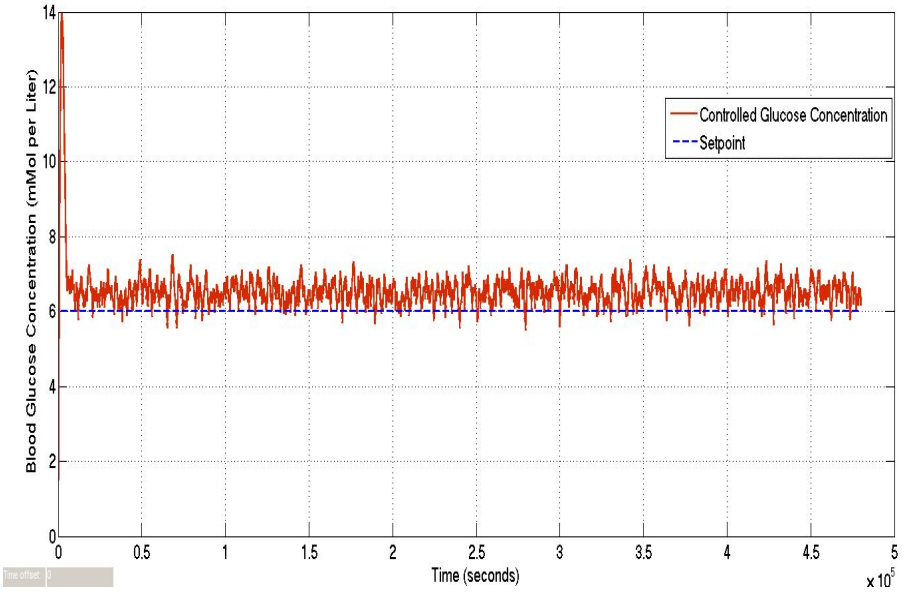


Figure 5.9: Response of Adaptive Backstepping Controller Subjected to Noise

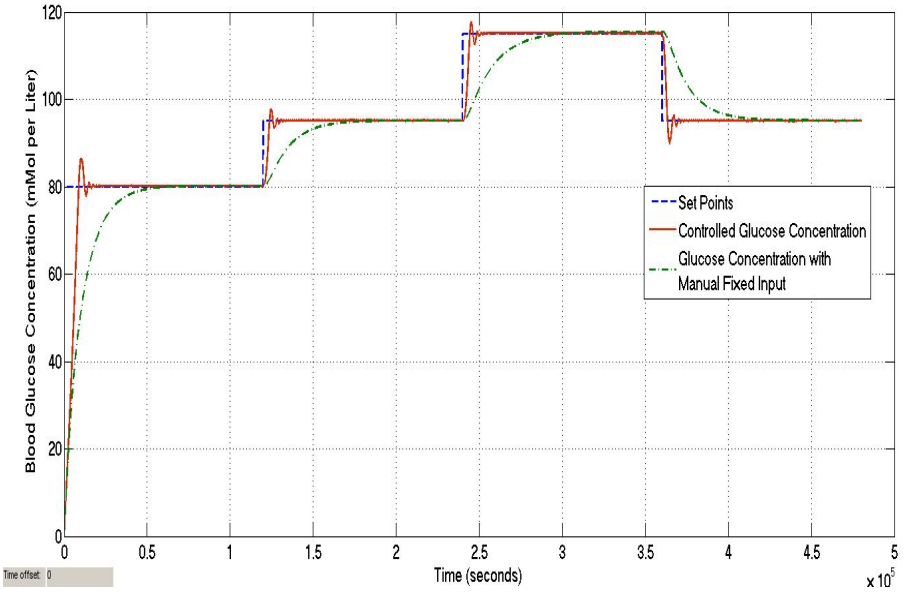


Figure 5.10: New Setpoints Tracking

model based fuzzy-PI and genetic fuzzy-PI controllers [45], [17]. Comparison is made from simulation results of controllers for four similar setpoints. From maximum convergence time column, we see that using proposed controller settling time is reduced significantly. In fact, it is less than half the convergence times of fuzzy-PI and genetic fuzzy-PI controllers. Maximum overshoot from desired concentration level is 6.5, as shown in Fig. 10, which is less than fuzzy-PI and is slightly higher than genetic fuzzy-PI but within an acceptable range. Finally, steady state error is also zero with proposed controller.

### 5.2.4 Conclusion

From mathematical and simulation results we conclude that with adaptive backstepping based nonlinear controller we can achieve global exponential stability for glucose-insulin system. Therefore it can be used for treatment of type 1 diabetes patients to replace linear controllers.

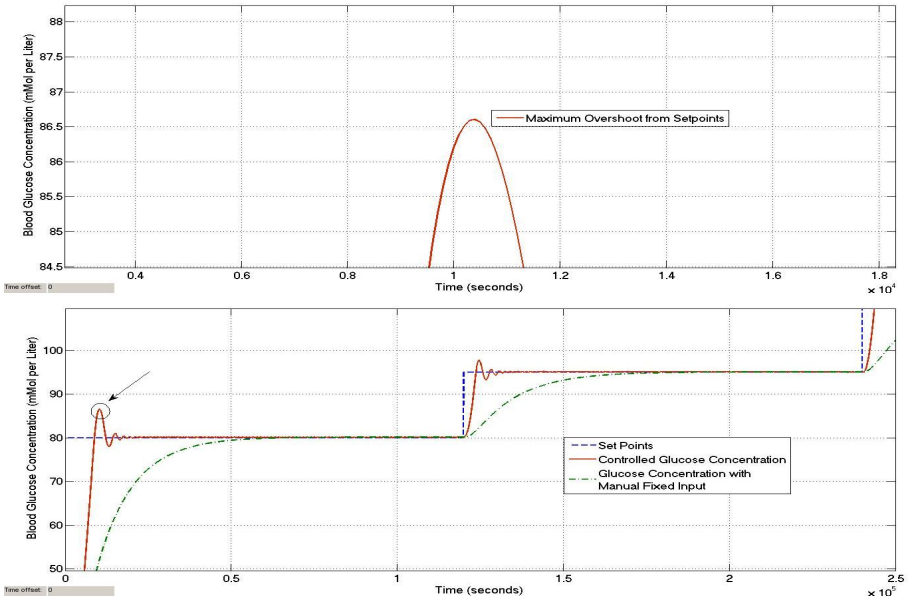


Figure 5.11: Maximum Overshoot

Table 5.1: Comparison of Control techniques

| Controller Type | Max. Convergence Time (minutes) | Max. overshoot | Steady State Error |
|---|---|---|---|
| Adaptive Backstepping Controller | 335 | 6.5 | No |
| Genetic Fuzzy-PI | 1000 | 3 | No |
| Fuzzy-PI | 1000 | 9 | Yes |

# Chapter 6

# Conclusion/Future Works

## 6.1 Conclusion

Linear controllers applied on nonlinear systems generally cannot produce as good results as nonlinear controllers when global behavior of system is under consideration. In our work, a nonlinear adaptive backstepping based controller is proposed to control glucose level in blood which is characterized by a nonlinear model. This new controller provides significant reduction in convergence time as compared to linear approaches. Adaptive backstepping algorithm and Lyapunov stability theory are used for derivation of controller which results in global exponential convergence of system to setpoints. Simulations obtained in SIMULINK support the mathematically derived results. Finally a comparison of proposed controller is made with fuzzy-PI and genetic fuzzy-PI controllers which indicates notable improvements in results.

## 6.2 Future Work

- Lypunov redesign controller for automatic infusion of insulin.
- Passivity based controller for automatic infusion of insulin.
- Backstepping based controller for a more detailed six state model.
- Hardware implementation of proposed nonlinear controllers.

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