Optimal Blood Glucose Regulation using Single Network Adaptive Critics

Sk. Faruque Ali and Radhakant Padhi

Abstract— **Diabetes is a serious disease during which the body's production and use of insulin is impaired, causing glucose concentration level to increase in the bloodstream. Regulating blood glucose levels as close to normal as possible, leads to a substantial decrease in long term complications of diabetes. In this paper, an intelligent neural network on-line optimal feedback treatment strategy based on nonlinear optimal control theory is presented for the disease using subcutaneous treatment strategy. A simple mathematical model of the nonlinear dynamics of glucose and insulin interaction in the blood system is considered based on the Bergman's minimal model. A glucose infusion term representing the effect of glucose intake resulting from a meal is introduced into the model equations. The efficiency of the proposed controllers is shown taking random parameters and random initial conditions in presence of physical disturbances like food intake. A comparison study with linear quadratic regulator theory brings out the advantages of the nonlinear control synthesis approach. Simulation results show that unlike linear optimal control, the proposed on-line continuous infusion strategy never leads to severe hypoglycemia problems.**

I. INTRODUCTION

The idea of using mathematical control theory to solve problems in biological sciences is relatively old [1–3]. However, in recent years activities based on this idea is growing fast. This is primarily due to development of more mathematical models for various biological systems [1], [2]. This rapid growth can also be attributed to the advancement in control theory. Some of the recent biomedical applications of control engineering can be found in [2] and the references therein. In the present study an attempt has been made to regulate blood glucose concentration in diabetic patients using nonlinear optimal control approach.

Diabetes is a disease in which the blood sugar level increases in patients and a significant effort is directed towards finding better ways to manage diabetes. The normal blood glucose concentration level in human is in the narrow range of $70 - 110$ mg/dl. Higher blood sugar level leads to hyperglycemia and low blood sugar level results in hypoglycemia. This concentration is normally controlled within these limits by hormones like, insulin and glucagon. Blood glucose concentration is elevated because of deficient insulin secretion or abnormal insulin action. Traditionally, managing diabetes has been through intermittent monitoring of blood glucose and then administering an appropriate dose of insulin into the blood stream. This method of intermittent monitoring and administration of insulin cannot ensure blood glucose remains at near normal levels at all times and therefore, there is considerable interest in managing diabetes on a continuous basis [3], [4] using subcutaneous glucose measurements.

An alternative approach is to replicate the function of pancreatic insulin, i.e., a continuous measurement and continuous insulin injection to the body based on a feedback strategy using an external device such as a pump [3–7]. This pump that acts like an artificial pancreas would include a sensor and an insulin container. The sensor provides the measurements of the blood glucose concentration and passes the information to a feedback control system that would decide on the necessary insulin delivery rate using control algorithms to keep the patient under metabolic control. The pump injects insulin through a catheter placed under the patients skin.

Robustness to parameter uncertainties and external disturbances, should be satisfied before installing any automatic system of drug delivery. Therefore, it is vital for the patients that controller used in the closed loop system should be capable of handling these uncertainties in parameters. In this study we apply a nonlinear optimal control approach using neural networks, a single adaptive critic network, to monitor blood glucose concentration.

Several methods have been previously employed to design the feedback controller for insulin delivery, such as classical linear control [4]; and pole placement [3], where a linearized model of the system is used for the design. Model predictive control (MPC) [5], [6] and higher order sliding mode (HOSM) control [7], [8]. Hypoglycemia (blood glucose level below 50 mg/dl) is a major concern with many of these controllers [7] (it will be shown later for a linear controller case), whereas HOSM increases model complexity.

Many difficult real-life control problems can be formulated within the framework of optimal control. It is well known that the dynamic programming formulation offers the most comprehensive solution approach to nonlinear optimal control in a state feedback form [9]. However, a huge (infeasible) amount of computational and storage requirements are needed. An innovative idea of 'Approximate Dynamic Programming' (ADP) has been proposed in [10] to get around the computational complexity. In this paper ADP is attempted using a "Single Network Adaptive Critic" (SNAC) [11]. The SNAC architecture offers three potential advantages: a simpler architecture, lesser computational load and reduced approximation error than Adaptive Critic Networks [10]. The efficiency of the technique has been

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reported for a class of nonlinear systems [12], treatment of Perturient Paresis in Cows [11], etc. In the present study we apply SNAC to regulate blood glucose concentration in diabetic patients. The advantages of using SNAC is it provides nonlinear optimal treatment strategy for diabetic patients. It can be implemented online. Furthermore, through simulation results (shown later in section IV), it is observed that unlike linear quadratic controller, SNAC does not lead to any hypoglycemic conditions.

The paper is organized as follows: Section II deals with the mathematical modeling aspects of the problem. Nonlinear Minimal model is considered for the present analysis with exogenous glucose intake as food. In Section III we discuss the necessary conditions of optimality from a discrete dynamic programming perspective. We describe the main idea of a neural network based controller synthesis procedure in this section. Results from the simulation studies are discussed next in Section IV and derive some conclusions in Section V.

II. MATHEMATICAL MODEL FOR INSULIN-GLUCOSE REGULATION

In this paper, the insulin-glucose regulatory system dynamics in the human body as described by the "Minimal Model" is used. Bergman minimal model [13], [14] is a commonly referenced model in the literature and approximates the dynamic response of a diabetic patients blood glucose concentration to the insulin injection using nonlinear differential equations.

A. Minimal Model for Insulin-Glucose Regulation

Minimal model is composed of two parts, first part describes the glucose plasma concentration considering the dynamics of glucose uptake and independent of circulating insulin. It has treated insulin plasma concentration as a known forcing function [3].

$$\begin{aligned} \dot{G}(t) &= -p_1\left[G(t)-G_b\right]-X(t)G(t)+D(t) \\ \dot{Z}(t) &= -p_2X(t)+p_3\left[I(t)-I_b\right] \end{aligned} \tag{1}$$

where $t=0$ shows the time glucose enters blood, $G(t)$ is the glucose concentration in the blood plasma in (mg/dl), $Z(t)$ is the insulins effect on the net glucose disappearance (1/min). G_b is the basal pre-injection level of glucose in (mg/dl). Parameter p_1 is the insulin-independent rate constant of glucose uptake in muscles and liver in (1/min), p_2 is the rate for decrease in tissue glucose uptake ability (in 1/min), p_3 is the insulin-dependent increase in glucose uptake ability in tissue per unit of insulin concentration above the basal level in $((\mu\text{U/ml})^{-1}\ \text{min}^{-2})$.

Insulin kinetics is given by a single equation which describes the plasma insulin concentration considering the dynamics of pancreatic insulin release in response to the glucose stimulus [3].

$$\dot{I}(t) = -n\left[I(t)-I_b\right] \tag{2}$$

$I(t)$ is the insulin concentration in plasma at time t in (μU/ml), I_b is the basal pre-injection level of insulin in (μU/ml). n is the first order decay rate for insulin in blood (1/min). It is worth noting that all the values are calculated for a person of average weight and these are not constant numbers and vary from patient to patient, which makes the design of the controller a more challenging task.

To show the complete dynamics of the glucose-insulin regulatory system, a food intake term is considered in Eq. 1. However, typically a diabetic person quantifies the food disturbance in terms of gram carbohydrate (CHO) it contains. Since, CHO contain of food varies with food types and patient habit, we represent the food intake in a patient in terms of glucose added in the blood due to the meal intake. Relation between the food CHO contain and the amount of glucose added into the blood can be obtained from the ref. [15]. $D(t)$ shows the rate at which glucose is absorbed to the blood from the intestine, following food intake. This disturbance can be modeled by a decaying exponential function, whose dynamics is given by the following equation [3], [16], [8].

$$\dot{D}(t) = -BD(t), \quad B>0 \tag{3}$$

where t is in (min) and $D(t)=Aexp(-Bt)$ is in (mg/dl/min) with $t>0$.

The objective of the study is to develop a nonlinear control technique to compensate the uncertainties and disturbances and to stabilize the blood plasma glucose concentration of a diabetic patient at the basal value. It should be noted that the control term is not yet considered in the model introduced in Eq. 2.

B. Model for control design

The system of equations introduced in Eqs. 1-3 can be combined to get following equations

$$\begin{aligned} \dot{x}_1 &= -p_1\left[x_1-G_b\right]-x_1x_2+x_4 \\ \dot{x}_2 &= -p_2x_2+p_3\left[x_3-I_b\right] \\ \dot{x}_3 &= -n\left[x_3-I_b\right]+u(t) \\ \dot{x}_4 &= -Bx_4 \end{aligned} \tag{4}$$

In Eq. 4, x_1,x_2,x_3, and x_4 represent $G(t)$, $X(t)$, $I(t)$ and $D(t)$ respectively. $u(t)$ is the control variable. It defines the insulin injection rate and replaces the normal insulin regulation of the body [8].

The aim of the present study is to design the control system such that the system variables in Eq. 4 reach their equilibrium values (i.e., basal values in the present case). Therefore, for convenience, system dynamics is rewritten in its deviation terms. For this we define,

$$\begin{bmatrix} x_1 & x_2 & x_3 & x_4 \end{bmatrix}^T = \begin{bmatrix} x_{1_0} & x_{2_0} & x_{3_0} & x_{4_0} \end{bmatrix}^T + \begin{bmatrix} x_{1_d} & x_{2_d} & x_{3_d} & x_{4_d} \end{bmatrix}^T \tag{5}$$

where $\begin{bmatrix} x_{1_d} & x_{2_d} & x_{3_d} & x_{4_d} \end{bmatrix}^T$ is the deviated state about the equilibrium point $\begin{bmatrix} x_{1_0} & x_{2_0} & x_{3_0} & x_{4_0} \end{bmatrix}^T$ of the system. From Eq. 4 the equilibrium is obtained as

$$\begin{bmatrix} x_{1_0} & x_{2_0} & x_{3_0} & x_{4_0} \end{bmatrix}^T = \begin{bmatrix} G_b & 0 & I_b & 0 \end{bmatrix}^T \tag{6}$$

C. Model with normalized variables

For better training of neural networks (see Section III-B), we normalize the neural network inputs. For this reason, we define the new variables $\bar{x_1} \triangleq x_{1_d}/x_{1_n}$, $\bar{x_2} \triangleq x_{2_d}/x_{2_n}$, $\bar{x_3} \triangleq x_{3_d}/x_{3_n}$, $\bar{x_4} \triangleq x_{4_d}/x_{4_n}$, where, subscript $(_n)$ denotes nominal values of the variables. After writing the system dynamic equations in terms of the normalized variables and then for convenience redefining $[x_1\ x_2\ x_3\ x_4]^T \triangleq [\bar{x_1}\ \bar{x_2}\ \bar{x_3}\ \bar{x_4}]^T$, following equations are obtained.

$$\left\{\begin{array}{c}\dot{x}_1\\ \dot{x}_2\\ \dot{x}_3\\ \dot{x}_4\end{array}\right\} = \left\{\begin{array}{l}-p_1x_1-(x_1+G_b/x_{1_n})x_2x_{2_n}+x_4x_{4_n}/x_{1_n}\\ -p_2x_2+p_3x_3x_{3_n}/x_{2_n}\\ -nx_3+\bar{u}(t)\\ -Bx_4\end{array}\right\} \tag{7}$$

Note that the equilibrium point of the homogeneous system dynamics in (7) now corresponds to the origin (for normalized and deviated states) and the control term $\bar{u}(t) = u(t)/x_{3_n}$ represents the normalized rate of insulin infusion. For convenience let us represent $(u(t) = \bar{u}(t))$.

Equation (7) can be rewritten in state space form as

$$\dot{X} \quad = F(X,\ u) \quad = f(X)+g(X)u(t) \tag{8}$$

where, $X = [x_1\ x_2\ x_3\ x_4]^T$.

Note that the control term appears only in the insulin dynamics, i.e., only the rate of insulin injection is modified by the state feedback control theory. Since only the plasma glucose concentration has to reach it basal value, a output regulator problem is considered for the medication problem. The output (y) is considered as the following

$$y = CX = [1\ 0\ 0\ 0]X \tag{9}$$

III. OPTIMALITY CONDITION AND NEURAL NETWORK SYNTHESIS

A. Optimality Conditions

For use with neural networks, the insulin-glucose regulation medication dynamics is first discretized as (in Euler integration form [17])

$$X_{k+1} = X_k + \Delta t\ F^k(X_k, u_k) \tag{10}$$

where Δt is the step size in time. The discretized output vector (y_k) is given as

$$y_k = CX_k = [1\ 0\ 0\ 0]X_k \tag{11}$$

A standard regulator cost function with output weighting is considered. An approximate (using trapezoidal rule [17]) discrete cost function is obtained.

$$J = \frac{1}{2}\sum_{k=1}^{N\to\infty}[y_k(Q_d)y_k + u_k(R_d)u_k] \tag{12}$$

where $Q_d = Q\Delta t \geq 0$, $R_d = R\Delta t > 0$ are the weighting matrices on state and control respectively and Δt is the step size in time. Appropriate choice of these values is problem dependent and can be adjusted with relative ease after a few simulations. Applying the standard discrete optimal control theory [9], [11], the equations for optimal control and costate dynamics are given by

$$u_k = -R^{-1}[0\ 0\ 1\ 0]\lambda_{k+1} \tag{13}$$

$$\lambda_k = \lambda_{k+1} + \Delta t\left[C^TQC\ X_k + \left(\frac{\partial F^k}{\partial X_k}\right)^T\right] \tag{14}$$

where, λ_k is the costate variable at time step t_k, the dynamics for which evolves backwards in time.

At each time step k the coupled equations (8, 10, 13 and 14) have to be solved simultaneously, together with the boundary conditions (X_1 specified and $\lambda_N = 0$ as $N \to \infty$), to obtain the optimal control solution u_k.

B. Procedure for Neural Network Synthesis

In this section, a neural network based optimal control synthesis is presented. The schematic of the controller synthesis procedure is shown in Fig. 1. We propose a neural network structure that solve the optimal control problem. The controller is essentially obtained through what we call as a set of "critic networks".

The simulation for blood glucose regulation problem is run for two different cases. In the first case the model parameters (p_1, p_2, p_3, n, B, etc.) are assumed to be constant and only the initial conditions of the state variables are changed. This simulation refers to a particular patient whose physiological parameter are assumed to be unchanged. But in practical situation, patients will have different physiological characteristics and therefore the model parameters will differ from individual to individual. To design a control system that can consider a varied range of patient, a second case is consider, where the model parameters (like, p_2, p_3, n, B) are also varied (p_1 is not varied as p_1 is assumed zero for diabetic patients, see [3] for details).

1) State generation for neural network training:: In the controller synthesis process, we first fix a particular time step k. Then, we choose a set of states $S = \{X_k : X_k \in \text{Domain of interest}\}$ for which the critic networks are to be trained. Obviously it is a difficult task, mainly because of the fact that, we do not know how exactly a system evolves in the presence of control. It may contain very large values to zero near steady state conditions. For this reason, we follow a telescopic procedure outlined below.

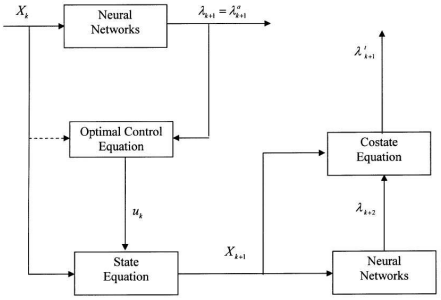

Fig. 1. Schematic of optimal control synthesis using neural networks

Define, for $i = 1,2,3,\ldots, S_i = \{$ all $X_k : \|X_k\|_\infty \leq c_i\}$, where c_i is a positive constant. Notice that for $c_1 \leq c_2 \leq c_3 \leq \cdots$, $S_1 \subseteq S_2 \subseteq S_3 \subseteq \cdots$. Thus, for some $i = I$, S_I will include the domain of interest for initial conditions. Hence, to begin the synthesis procedure, we fix a small value for the constant c_1 and train the networks for the states, randomly generated within S_1. Once the critic networks converge for this set, we choose c_2 close to c_1 and again train the networks for the profiles within S_2 and so on. We keep on increasing the constant c_i this way until the networks are trained for states in S_1. In this paper, we have chosen $c_1 = 0.05$, $c_i = c_1 + 0.01(i-1)$ for $i = 2,3,\ldots$ and continued until $c_i = c_I = 1$.

2) Neural network training:: The critic neural network(s) essentially capture the relationship between X_k and λ_{k+1}. For faster training, we have synthesized four neural networks (separate networks for each element of the vector λ_{k+1}). Discussion for the training in second case is presented here as it is more complicated. We have assumed that the parameters of the problem (p_2, p_3, n, B) can vary, within known minimum and maximum values. Thus, $p_2 \in [p_{2\ min},\ p_{2\ max}]$, $p_3 \in [p_{3\ min},\ p_{3\ max}]$, $n \in [n_{min},\ n_{max}]$, and $B \in [B_{min},\ B_{max}]$. Thus, to capture the relationship between X_k and λ_{k+1}, we construct an augmented vector $X_k^{inp} = \left[X_k^T \vdots P^T\right]^T$ (P is the vector containing parameters), which serves as the input to the neural networks. However, since the individual elements of X_k^{inp} vary widely in magnitude, we construct a normalized vector to serve as the input. Thus we have $X_k^{inp} = [z_{1k}\ z_{2k}\ z_{3k}\ z_{4k}\ p_2/p_{2_n},\ p_3/p_{3_n},\ n/n_n,\ B/B_n]^T$, where p_{2_n}, p_{3_n}, n_n and B_n are the normalizing values for p_2, p_3, n and B respectively. Note that after successful training of the networks, we can directly calculate the associated optimal control v_k from Eq. 13 for each X_k^{inp}. We synthesize the neural networks in the following manner (Fig. 1).

1) Generate S_i, as described in Section III-B.1.
2) For each element X_k of S_i, follow the steps below,
   - construct X_k^{inp},
   - input X_k^{inp} to the networks to get λ_{k+1}: let us denote this actual output as λ_{k+1}^a as well,
   - calculate v_k, knowing X_k and λ_{k+1}, from optimal control equation Eq. 13,
   - get X_{k+1} from the state equation (10, 8), using X_k and u_k,
   - construct X_{k+1}^{inp},
   - input X_{k+1}^{inp} to the networks to get λ_{k+2},
   - calculate the target λ_{k+1}, from the costate equation Eq. 14. Let us denote this as λ_{k+1}^t.
3) Train the networks, with all X_k^{inp} as input and all corresponding λ_{k+1}^t as output.
4) Check for convergence, as described in subsection III-B.3.
5) If proper convergence is achieved, stop and revert to step-1, with $i = i+1$. If not, go to step-1 and retrain the networks.
6) Continue the process till $i = I$; i.e., until $c_i = c_I = 1$.

TABLE I
PARAMETER VALUES FOR CASE-I STUDY

Parameter	Value	Parameter	Value
p_1	0	p_2	0.0142
p_3	1.54×10^{-5}	B	0.05
n	0.2814	γ	0
G_b	70 mg/dl	I_b	7 μU/ml

One can notice that for faster convergence, one can take the convex combinations $\left[\beta\lambda_{k+1}^t + (1-\beta)\lambda_{k,j+1}^a\right]$, $\left[\beta\lambda_{2k+1}^t + (1-\beta)\lambda_{2k,j+1}^a\right]$ as target outputs for training, where $0 < \beta < 1$ is the learning rate for the neural network training. For the biomedical problem under consideration, we have followed these ideas (selecting $\beta = 0.5$).

3) Convergence condition:: Before changing c_i to c_{i+1} and generating new profiles for further training, it should be assured that proper convergence is arrived for c_i. This is not discussed here and can be found in [11].

4) Choice of neural network structure and initialization:: The choice of a network is a trade-off between accuracy and computational complexity. For this particular problem, we took four $\pi_{4,6,4,1}$ neural networks, one each for each of the costates for case-I. Similarly, for random parameters and states four $\pi_{8,6,4,1}$ neural networks, one each for each of the costates, is considered. *Tangent sigmoid* function is considered for all the hidden layers and *linear* function for the output layer.

IV. NUMERICAL RESULTS AND DISCUSSIONS

Two cases are considered in the present study. First, different conditions of a patient are considered. In this case the physiological properties of patient are assumed to remain same and therefore the model parameters are not changed. In the second case random model parameters and random initial states are considered. This replicates a situation where there are many patients each with a different physiological property. This situation represents the reality better and also shows the efficiency of the control design over a broad class of patient parameters. A comparison with linear quadratic regulator control technique applied to the nonlinear system dynamics is also provided.

A. Case-I: Parameter Values

For simulation study and training of the network in case-I, the model parameters considered are shown in Table I.

For all simulation studies, the basal value of glucose (G_b) and insulin (I_b) concentrations in plasma are considered as 70 mg/dl and 7 μU/ml respectively (see Table I). For the neural network training purposes, the range of values for the state variables are shown in Table II. where the normalizing variables $[x_{1_n},\ x_{2_n},\ x_{3_n},\ x_{4_n}]^T$ are taken as $[150,\ 0.01,\ 100,\ 10]^T$. The time interval Δt is chosen as 0.5 seconds (studies with with higher time step (10s) is underway). The output weight Q is taken as $0.01 \times (x_{1_n})^2$ and the control weight is considered as $3000 \times (x_{3_n})^2$.

TABLE II

RANGE OF VALUES FOR STATE VARIABLES

state	Value	state	Value
$x_{1\ min}$	$0/x_{1_n}$	$x_{1\ max}$	$300/x_{1_n}$
$x_{2\ min}$	$-0.01/x_{2_n}$	$x_{2\ max}$	$0.03/x_{2_n}$
$x_{3\ min}$	$-10/x_{3_n}$	$x_{3\ max}$	$300/x_{3_n}$
$x_{4\ min}$	$0/x_{4_n}$	$x_{4\ max}$	$20/x_{4_n}$

B. Case-I: Analysis of Simulation Results

The parameters mentioned in subsection IV-A leads to an unstable glucose trajectory as shown in Fig. 2 for untreated (i.e., without exogenous insulin supply) conditions. Figure 2 also shows the glucose profile for both linearized system and nonlinear system with linear quadratic control (LQR) and single network adaptive critic control (SNAC). It is evident form Fig. 2 that linearized system and nonlinear system differs in their profiles. It also to be noted that SNAC based nonlinear control performs better than LQR based control. The glucose profiles in LQR based control strategy brings down the glucose in the patient body to 50 mg/dl (a major concern for diabetic patients [3]). This is absent in neural medication. Figure 3 shows the profile of insulin concentration in the patient. The control required (or the rate of exogenous insulin injection) is shown in Fig. 4. One can stop neural medication at 200 minutes of simulation as the control required after that is zero.

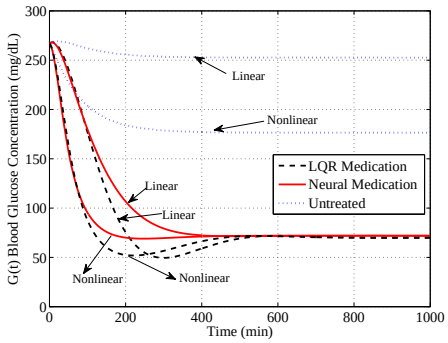

Fig. 2. Open and closed loop Glucose regulatory system, $(X(0) = [1.31\ 0.31\ 1.82\ 0.064]^T)$

Plasma glucose concentrations with random initial conditions and parameters as given in Table I are shown in Fig. 5. Figure 5 shows the glucose trajectories for untreated patients and for patients with neural medication together. As shown in Fig 5 neural medication never lead to hypoglycemic condition where the glucose concentrations goes below 50 mg/dl. It is to be noted that all glucose profiles are bought down to the basal value (70 mg.dl) within 200 minutes of simulation even for the hypoglycemia cases. The corresponding rate of insulin injection are shown in Fig. 6.

C. Case-II: Parameter Values

In second case the parameters (P_2, p_3, n and B) are also considered random. For the neural network training purposes,

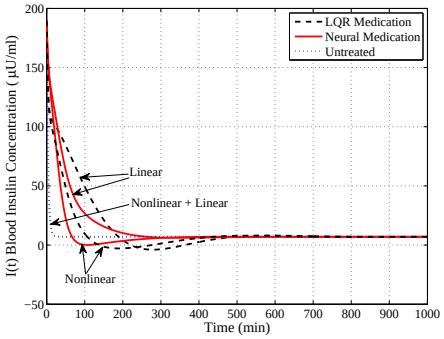

Fig. 3. Open and closed loop Insulin profile

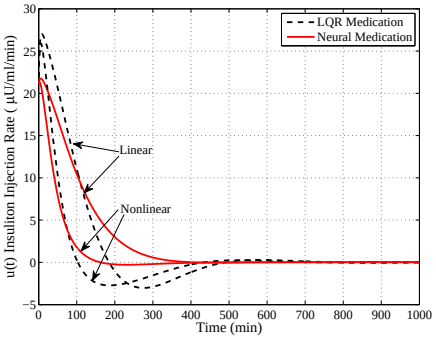

Fig. 4. Insulin injection rate required for Glucose regulation

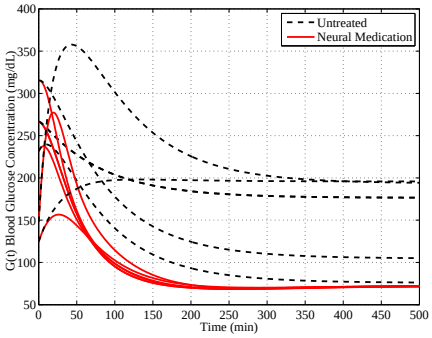

Fig. 5. Glucose trajectories with random initial conditions

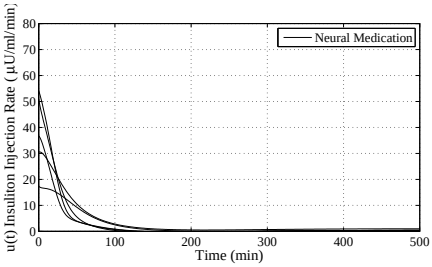

Fig. 6. Insulin injection rate for random initial conditions

TABLE III

RANGE OF VALUES FOR PARAMETERS

state	Value	state	Value
$p_{2\ min}$	$0.01/p_{2_n}$	$p_{2\ max}$	$0.02/p_{2_n}$
$p_{3\ min}$	$1\times10^{-6}/p_{3_n}$	$p_{3\ max}$	$20\times10^{-6}/p_{3_n}$
n_{min}	$0.30/n_n$	n_{max}	$0.12/n_n$
B_{min}	$0.1/B_n$	B_{max}	$0.01/B_n$

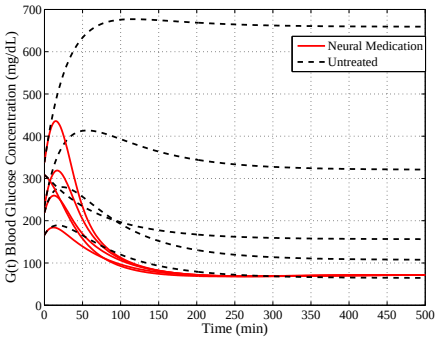

Fig. 7. Glucose trajectories with random parameters

we have assumed range for the state variables (X_k) as given in Table II and range for the rest of the parameters is given in Table III.

The normalizing variables in Table III $([p_{2_n},\ p_{3_n},\ n_n,\ B_n]^T)$ are taken as $\left[0.015,\ 5\times10^{-6},\ 0.21,\ 0.05\right]^T$. Blood glucose concentration with random model parameters are shown in Fig. 7. The simulated glucose profiles without treatment and with neural treatment are shown together for better comparison. The controlled glucose trajectories are observed to reach basal value in short time. The corresponding control inputs (rate of insulin injection) are shown in Fig. 8. As shown in Fig. 7, the insulin injections can be stopped after 100 minutes as all the control trajectories are seen to reach zero within this time.

V. CONCLUSIONS

One of the challenging control problems in human regulatory systems, the diabetes management, has been discussed in the present study. The treatment of the disease using linear optimal controller applied to nonlinear system and through SNAC based neural medication has been considered. Two different training cases are studied. The first case considered a patient with various physiological conditions and in the second case the neural controller is trained for random model parameter, which represents different patients. The second case is more realistic and also shows the robustness of the neural control under parameter variation. In both the cases neural control shows rapid settlement of blood glucose concentrations to its basal value. Furthermore, a comparison study with the linear quadratic regulator theory clearly brings out the advantage of the proposed nonlinear control synthesis approach.

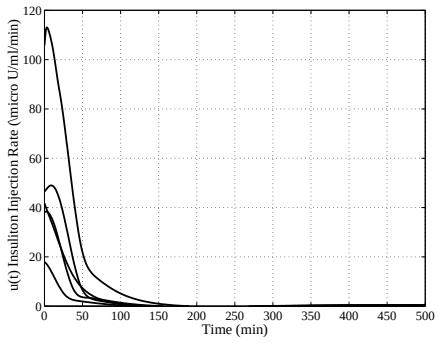

Fig. 8. Insulin injection rate for random parameters

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