# DESIGN OF TWO CONTROLLERS BASED ON DMRAC AND MIT METHODS ON GLUCOSE-INSULIN SYSTEM

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***ABSTRACT***

*This paper presents a closed-loop control system with regulating blood glucose level in type-1 diabetic patients. The contribution of this paper is twofold for controlling the glucose level in insulin. Firstly a direct model reference adaptive control algorithm (DMRAC) for the glucose insulin system is considered based on the command generator tracker (CGT). Secondly, another significant control MIT adaptive control method (MITC) is desired to obtain a comparative study between the two proposed controllers. The achievement of our study is to affect these two algorithms for the regulation of the glucose level in type 1 diabetes, because the problem of the diabetes is one of the largest difficulties necessities a methods for treating the disease. Diabetes is a malfunction in the glucose-insulin system; so ours controllers can successfully assure that the blood glucose levels should be maintained between 80 mg/dl and 120 mg/dl before meals; less than 180 gm/dl after meals. The application of these controllers is tested in silico for effective diabetic I patients. The simulations demonstrate that the developed algorithms lead to an asymptotically stable error and illustrate the validity of the algorithms.*

***KEYWORDS***

*Adaptive control, DMRAC, MITC, Glucose-insulin system, Type I diabetes.*

## 1. INTRODUCTION

Diabetes mellitus is a widespread disease. According to the World Health Organization (WHO), globally in 2013 approximately 382 million people suffered from diabetes world-wide and more than 80% of people with diabetes live in low-and middle-income countries. For 2030, an augmentation to 552 million patients is prognosed by the International Diabetes Federation [1]. The diabetes is a severe disease that occurs when the body has difficulty regulating the quantity of glucose in the blood stream. Therefore, people with type 1 diabetes must take daily insulin injections to survive [2]. To avoid patients having to establish each insulin quantity manually, and to limit the vast variation in blood glucose concentration, an artificial pancreas needs to be developed as an important scientific research aim. The primary idea is to calculate the required insulin dose using a control algorithm based on continuous glucose measurements, which are obtained via a sensor without human input. So it is necessary to use an appropriate control for these patients.

Most diverse control algorithms for regulating blood glucose level techniques have been proposed and often tested in silico via computer simulators [3, 4, 5]. One of the traditional controllers is PID controller [6, 7]. Like in several physical applications of PID control, Steil et al in [8] used a couple of PID controllers on the glucose-insulin system. One of the disadvantages of PID controller is that it is not considered the changes in patient's parameters which can vary from patient to patient. Our challenges in this study is that proposed two robust closed-loop controllers for blood glucose like the direct model reference adaptive control (DMRAC) and the adaptive MIT control.

The state of art of an adaptive control approach originated by Kaufman et al [9]. In this approach an asymptotic stability, this last is assured if the system is almost strictly positive real (ASPR); hence if there exists a gain K such that the closed-loop transfer function is strictly positive real (ASPR). This gain need not be physically realized during implementation. The important point in most of this paper is that proposed two controllers by employing direct model reference adaptive control and the adaptive MIT control with the regard to the complexity and the positivity on both the inputs and the output. Then we will control the insulin and the glucose level of the patient.

The paper is organized as follows. The glucose-insulin mathematical model is explained in Section 2. The design of the adaptive MIT control algorithm is explained in Section 3. Then the problem statement and proposed direct model reference adaptive control structure are shown in Section 4. Section 5 describes the application of the tow controllers on the mathematical model of the glucose - insulin dynamics, and then the test on patients, and gives simulation results with discussion. Finally, Section 6 presents concluding and future work.

## 2. GLUCOSE-INSULIN MATHEMATICAL MODEL

There are several researches that were already developed on the dynamics of the glucose-insulin, as in the model of Bolie, Hovorka and the model of Bergman; this last is widely used in recent years.

### 2.1. Bergman Model

The original glucose minimal model describes how the glucose level behaves according to measured insulin data during an IVGTT (the Intravenous Glucose Tolerance Test). This model is defined by these equations [10]:

$$\begin{aligned} \dot{G}(t) &= -(P_1 + X(t))\ G(t) + P_1 G_b + d(t) \\ \dot{X}(t) &= -P_2 X(t)) + P_3 (I(t) - I_b) \\ \dot{I}(t) &= -n\left[I(t) - I_b)\right] + u(t) \end{aligned} \tag{1}$$

Where $G(t)$ (mg/dL) is the blood glucose concentration. $I(t)$ (mU/L) the blood insulin concentration, and $X(t)$ (1/min) is the effect of active insulin.

Then $G_b$ (mg/dL) steady state blood glucose concentration (baseline). $I_b$ [mU/L] steady state blood insulin concentration (baseline).

Then in [11] the state space representation of the digestion dynamics is:

$$\begin{bmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \end{bmatrix} = \begin{bmatrix} -p_1 & -G_b & 0 \\ 0 & -p_2 & p_3 \\ 0 & 0 & -n \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} + \begin{bmatrix} 0 & 1 \\ 0 & 0 \\ 1 & 0 \end{bmatrix} \begin{bmatrix} u(t) \\ d(t) \end{bmatrix} \tag{2}$$

And $y = \begin{bmatrix} 1 & 0 & 0 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} + \begin{bmatrix} 0 & 0 \end{bmatrix} \begin{bmatrix} u(t) \\ d(t) \end{bmatrix}$

$x_1 = G(t)$, $x_2 = X(t)$, $x_3 = I(t)$

with $u(t)$ is the inputs, it represent the insulin infusion and $d(t)$ represent the meal perturbation.

Using $u(s)$ and $y(s)$ the Laplace transforms of $u(t)$ and $y(t)$, the transfer function model of the system to be written as:

$$y(s) = G_p(s)u(s) + G_d(s)d(s)$$

Where $G_p(s)$ is the transfer function of the system. $G_d(s)$ is the transfer of the meal disturbance.

## 2.2. Bolie Model [12]

The bio-mathematical Bolie model is simple and compatible. The model characterized the glucose- insulin system, it used a differential equations with four parameters: $\alpha$, $\beta$, $\delta$ and $\gamma$.

Where

$\alpha$: is the pancreatic insulin sensitivity to insulin.

$\beta$: represent the blood glucose concentration.

$\delta$: the tissue glycogen storage.

$\gamma$: the tissue glucose employ to high blood-glucose concentration.

The study described in this section will based on the bio-mathematical model of Bolie.

With reference to the blood glucose-insulin system, the corresponding first-order differential equations of the insulin and glucose regulatory sub-systems are given as [12.13].

$$\dot{x} = p - \alpha x + \beta y \tag{3}$$

$$\dot{y} = q - \gamma x - \delta y \tag{4}$$

The glucose ingestion $q$ is the input; then $y$ is the output of the blood glucose system, it is the blood glucose concentration. The blood insulin concentration $x$, and the insulin input $p$ can be derived from (5) to (8). Such that $\alpha$ $\beta$, $\delta$ and $\gamma$ are the parameters of the glucose-insulin system. From equations (3) and (4), we have:

$$y = -2\frac{\gamma}{\delta}x + \frac{2q}{\delta} - \frac{2}{\delta} \tag{5}$$

$$x = -\frac{\delta}{2\gamma}y + \frac{q}{\gamma} - \frac{1}{\gamma} \tag{6}$$

$$x = 2\frac{\beta}{\alpha}y + \frac{2p}{\alpha} - \frac{2}{\alpha} \tag{7}$$

$$p = \frac{\alpha}{2}x - \beta y + 1 \tag{8}$$

From equations (3) and (4), the differential equation for the glucose concentration $y$ designed without insulin infusion can be writing from (9).

$$\ddot{y} + \dot{y}(\alpha + \delta) + y(\alpha\delta + \beta\gamma) = \dot{q} + \alpha q \tag{9}$$

The differential equation of the second order insulin concentration for $x$ is derived as:

$$\ddot{x} + \dot{x}(\alpha + \delta) + x(\alpha\delta + \beta\gamma) = \beta q \tag{10}$$

The relationship between, glucose concentration is derived from (3) and (4).

## 3. DESIGN OF THE MODEL REFERENCE ADAPTIVE MIT CONTROLLER

In this section the closed-loop algorithm is determined and depends only on the one parameter regulating parameter $K$ of controller. The desired response of the reference model is $y_m$. Then the error between the system output $y_p$ and the reference output $y_m$ of the model can be selected as: $e = y_p - y_m$ . Note that the adaptive mechanism adjusts the controller parameters depends on the error value and the cost function selected in (11). The cost function determines the direction of the regulation made to the controller.

$$J(\theta) = \frac{1}{2}(y_p - y_m)^2 \tag{11}$$

For the output system track the reference trajectories in the closed loop, it is obvious to have a small value of $J$. Let us note that the minimization of the value of $J$ requires the change of this parameter in the form of the negative gradient as follows:

$$\frac{d\theta}{dt} = -\varphi \frac{\partial j}{\partial \theta} = -\varphi \frac{\partial e}{\partial \theta} \tag{12}$$

Where $\varphi$ determine the rate of adaptation and the partial derivative $\frac{\partial e}{\partial \theta}$ is called the sensitivity derivative of the system. Different cost function can be chosen:

$$J(\theta) = |e(\theta)| \tag{13}$$

with $\frac{d\theta}{dt} = -\varphi \frac{\partial e}{\partial \theta} sign(e)$

where $sign(e) = \begin{cases} 1, & e>0 \\ 0, & e=0 \\ -1, & e<0 \end{cases}$

From the above equations, the control *up* (*t*) *is* written in an actual form as follows. [14].

$$u_p(t) = K_p u_m(t)$$

$$y_p(t) - y_m(t) = G_p u_p(t) - G_m u_m(t)$$

Then $e = G_p K_p u_m - G_m u_m$

This expression was established by supposing that

$$y_p = G_p K_p u_m(t)$$

While the model reference is known, it can be easily find the derivative of the error

$$\frac{\partial e}{\partial K_p} = \frac{(s(\alpha_m + \delta_m) + (\alpha_m \delta_m + \beta_m \gamma_m))}{(s^2 + s(\alpha_m + \delta_m) + (\alpha_m \delta_m + \beta_m \gamma_m))} u_m$$

Next, we can find the adaptation law of adjustable parameter, therefore $K_p$ is defined according to the following adaptive rule

$$\frac{dK_p}{dt} = -\varphi e \frac{\partial e}{\partial K_p} = -\varphi e \frac{(s(\alpha_m + \delta_m) + (\alpha_m \delta_m + \beta_m \gamma_m))}{(s^2 + s(\alpha_m + \delta_m) + (\alpha_m \delta_m + \beta_m \gamma_m))} u_m$$

Where $\alpha_m, \beta_m, \gamma_m, \delta_m$ are the parametric values of the normal healthy model [15].

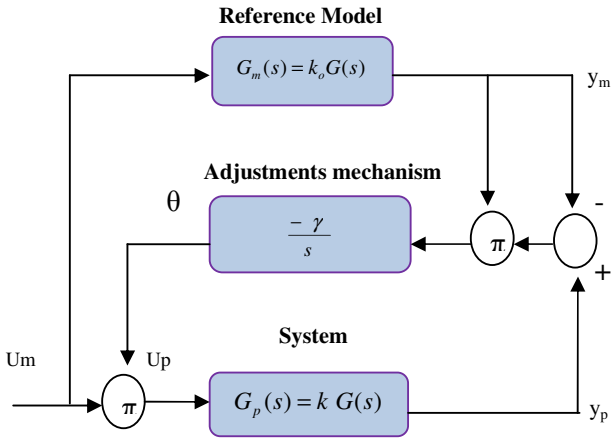


Figure. 1. Scheme of the reference adaptive control based on the MIT algorithm .

## 4. DESIGN OF THE DMRAC ALGORITHM CONTROLLER

The problem of DMRAC will be solved for the following equations of the process

$$\begin{aligned} \dot{x}_p(t) &= A_p x_p(t) + B_p u_p(t) \\ y_p(t) &= C_p x_p(t) \end{aligned} \tag{14}$$

Where $x_p(t)$ is the state vector, $u_p(t)$ is the control vector, $y_p(t)$ is the plant output vector, and $A_p$ , $B_p$ and $C_p$ are matrices with appropriate dimensions. The range of plant parameters is assumed to be known with

$$\underline{a}_{ij} \le a_p(i,j) \le \bar{a}_{ij}, i = 1...n, j = 1...m$$

$\underline{b}_{ij} \le b_p(i,j) \le \bar{b}_{ij}, i = 1..n, j = 1..m$

$a_p(i,j)$ is the $(i,j)^{th}$ element of $A_p$, and $b_p(i,j)$ is the $(i,j)^{th}$ element of $B_p$ .

The aim is to find a control $u_p(t)$ such as the outputs of the system $y_p(t)$ follow the output of reference model $y_m(t)$, this last is described

$$\dot{x}_m(t) = A_m x_m(t) + B_m u_m(t)$$
$$y_m(t) = C_m x_m(t)$$

$A_m$ , $B_m$ and $C_m$ are matrices with appropriate dimensions. The model is supposed stable. It is significant to note that the dimension of the state model can be made lower than that of the process, although both must have the similar number of output.

The model incorporates desired plant behaviour and in many cases $\dim[x_p(t)] >> \dim[x_m(t)]$.The adaptive control algorithm being presented is based upon the command generator tracker concept (CGT) developed by O'Brien and Broussard. [16].

To simplify the development of the control law, the concept of CGT at variable time is presented here. If a generating perfect tracking is reached, it means $y_p(t) = y_m(t)$ for $t \ge 0$, the trajectories of corresponding control and state are noted $x^*_p(t)$ and $u^*_p(t)$. The ideal system is such as it satisfies the same dynamics as that real system. Moreover, the output of the ideal system is identically stable at the output of the reference model, mathematically we have

$$\begin{bmatrix} x^*_p(t) \\ u^*_p(t) \end{bmatrix} = \begin{bmatrix} S_{11} & S_{12} \\ S_{21} & S_{22} \end{bmatrix} \begin{bmatrix} x_m(t) \\ u_m(t) \end{bmatrix}$$

Where the $S_{ij}$ sub matrices satisfy the following conditions

$$S_{11} A_m = A_p S_{11} + B_p S_{21}$$
$$S_{11} B_m = A_p S_{12} + B_p S_{22}$$
$$C_m = C_p S_{11} \ , \ 0 = C_p S_{12}$$

The adaptive control law based on this CGT approach is selected as [17]

$$u_p(t) = K_x(t) x_m(t) + K_u(t) u_m(t) + K_e(t)(y_m(t) - y_p(t)) \quad (15)$$

Where $K_e(t)$, $K_x(t)$ and $K_u(t)$ are adaptive gains and concatenated into matrix $K(t)$ as follows

$$K(t) = \begin{bmatrix} K_e(t) & K_x(t) & K_u(t) \end{bmatrix} \quad (16)$$

Defining the vector $r(t)$ as $r(t) = \begin{bmatrix} y_m(t) - y_p(t) \\ x_m(t) \\ u_m(t) \end{bmatrix}$.

The control $u_p(t)$ is written in a compact form as follows.

$$u_p(t) = K(t)r(t) \tag{17}$$

Where $K(t)$ is defined according to the following adaptive rule [18] as:

$$K(t) = K_I(t) + K_p(t)$$

Such that:

$$\dot{K}_I(t) = C_p(y_m(t) - y_p(t))r^T T\theta; K_I(0) = K_{I0}$$
$$K_p(t) = C_p(y_m(t) - y_p(t))r^T \bar{T}\theta$$

The diagram of the reference adaptive control based on the DMRAC algorithm is illustrated in figure2.

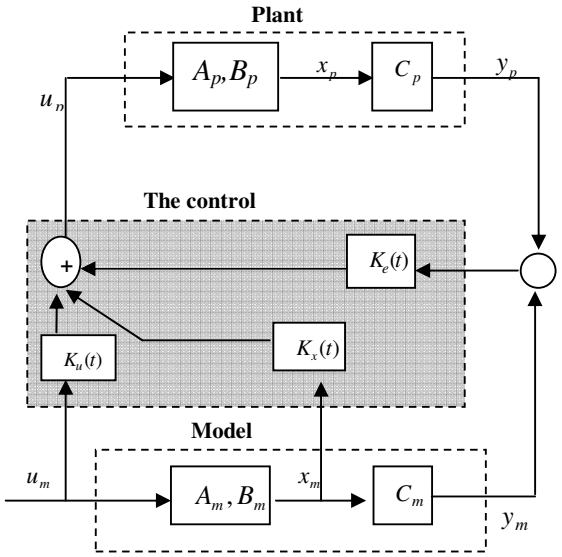


Figure. 2. Scheme of the reference adaptive control based on the DMRAC algorithm.

Sufficiency for asymptotic tracking is achieved if:

1. There exists a solution to the CGT problem,

2. The plant is ASPR (Almost strictly positive real); that is there exists a gain matrix $K_e(t)$, not needed for implementation, such that the closed-loop transfer function $G_c(s) = \left[I + G_p(s)K_e\right]^{-1} G_p(s)$ is SPR.

In general, the ASPR conditions are not satisfied by most real systems. Barkana and Kaufman [9] have remedied this situation by showing that a non-ASPR plant of the form $G_p(s) = C_p(SI - A_p)^{-1}B_p$ can be augmented with a feed-forward compensator $H(s)$ such that the augmented plant transfer matrix $G_a(s) = G_p(s) + H(s)$ is ASPR.

It was shown in [2] that in the resulting adaptive controller, the error between the model and the system is limited and small enough. Moreover, the gains will not be fixed but adaptive. The modification, incorporating the supplementary feed-forward into the reference model output, has been developed [18]. In [18] , asymptotic model following was achieved using a strictly proper stable feed-forward compensator . However it is also possible using a proper but not strictly proper stable feed-forward compensator [19].

The following theorem summarizes the stability of the approach DMRAC with augmented of the plant and the model.

**Theorem 1** [18]

Let us consider the adaptive controller given by (15), With the adaptive rule defined by equation (16), if the following designed conditions are satisfies, Then, the error output $y_p(t) - y_m(t)$ cancel yourself asymptotically and all the states and the profits will be limited. [17].

1. $G_a(s) = G_p(s) + H(s)$ is ASPR, where the transfer function of the plant is $G_a(s)$ and $H(s)$ is the transfer function of the compensator.

2. A solution exists for the system of equation CGT variable in time.

3. The compensator $H(s)$ is stable; it means $H(s)$ has all its proper values in the left half-plane.

## 5. SIMULATION RESULTS AND DISCUSSION

Simulation results of the model reference adaptive MIT control and DMRAC for the Bolie model of the glucose-insulin are given away in the following subsection (5.1), (5.2). Then the simulation results of the same tow controllers for the Bergman model are shown in subsection (5.3), (5.4).

### 5.1. Simulation Result with the MIT control on the Bolie Model

In this section we apply the MIT control .The results of this above described control idea are shown in Figure.3 to Figure.4.

Let the transfer function of the system glucose for a diabetic person for the Bolie model:

$$G_p(s) = \frac{s + \alpha}{s^2 + (\alpha + \delta)s + (\alpha\delta + \beta\gamma)}$$

Then let the transfer function of the system insulin for a diabetic person:

$$G_p(s) = \frac{\beta}{s^2 + (\alpha + \delta)s + (\alpha\delta + \beta\gamma)}$$

We note that for the simulation we considered the following values of systems parameters:

Table 1. The values considered for the simulation of the Bolie Model.

| The parameters | The normal person | The diabetic person |
|---|---|---|
| $\alpha$ | 0.05 | 2.25 |
| $\beta$ | 0.96 | 15.12 |
| $\gamma$ | 6.48 | 0.93 |
| $\delta$ | 1.76 | 0.12 |

It is clear that for the diabetic person, there is a reduced value of $\gamma$ which represents reduced sensitivity due to increased-resistance to insulin and an augmented value of $\beta$ which refers to the insulin release in response to the improved glucose concentration.

As our model bases, we considers the transfer function of the real system of glucose for a person in good health, it is considers a reference model.

By using the values of parameters for system of glucose-insulin, we obtained the transfer function of a healthy person and of a diabetic person. In this simulation system, the aim of the command is to join the system output to track their desired value.

Figure.3, and Figure.4 represent the outputs of the system and the reference model for the MIT control, i.e. the concentration of blood glucose for a healthy person (the reference model) and the concentration of blood glucose for a diabetic person (real system) for tow initial values considered in simulation 80mg/dl and 100 mg/dl. The perfect tracking is visible in permanent mode; the representation of input signal (the insulin infusion) is given in Figure. 5, we see that it is bounded.

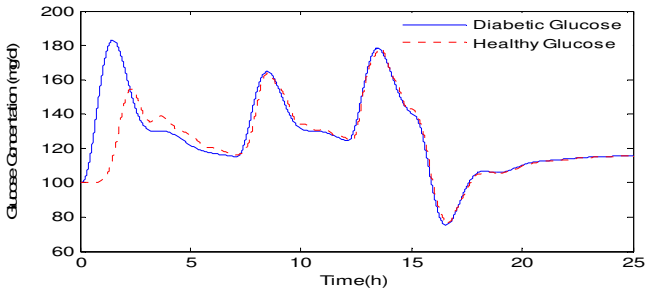


Figure.3. The outputs of the glucose concentration for a person in good health and a diabetic person for an initial value of 100 mg/dl for MIT control.

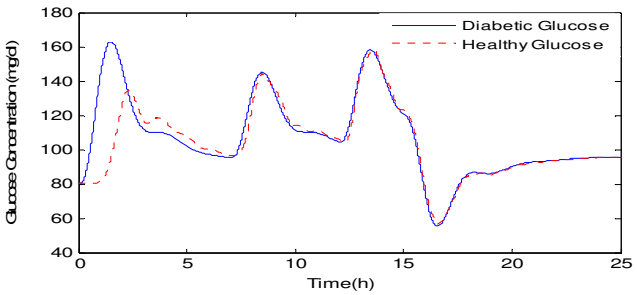

Figure.4. The outputs of the glucose concentration for a person in good health and a diabetic person for an initial value of 80 mg/dl for MIT control.

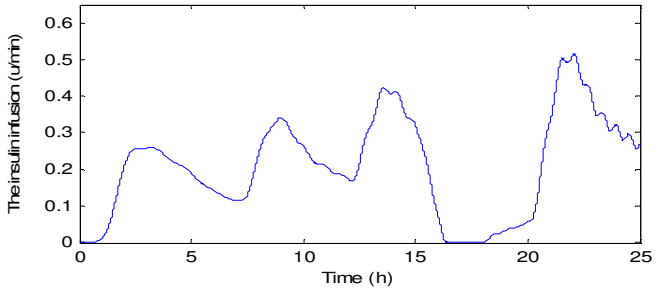


Figure.5. The control signal (the insulin infusion (u\min)).

## 5.2. Simulation Result with the DMRAC control on the Bolie Model

In this section we apply the control law (17). Simulation results of direct model reference adaptive control are shown in Figure.6 to Figure.8, such that the Figure.6 and Figure.7 represent the outputs of the system and the reference model for tow initial values considered in simulation 80mg/dl and 100 mg/dl. Then the representation of input signal is given in Figure. 8, we see that it is bounded.

The glucose insulin system for the tow cases of simulation of a healthy person and a diabetic person is of relative degree one and it is minimal phase, it is then ASPR (Almost Strictly Positive Real) and thus the error convergence is guaranteed. The application of this adaptive controller to the real system leads to an error asymptotically stable.

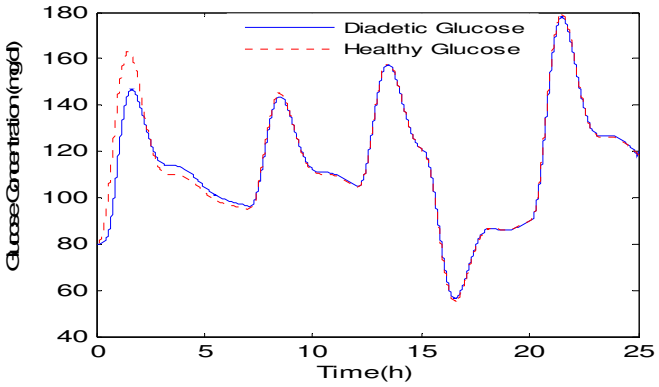


Figure.6. The outputs of the glucose concentration for a person in good health and a diabetic person for an initial value of 80 mg/dl for DMRAC control.

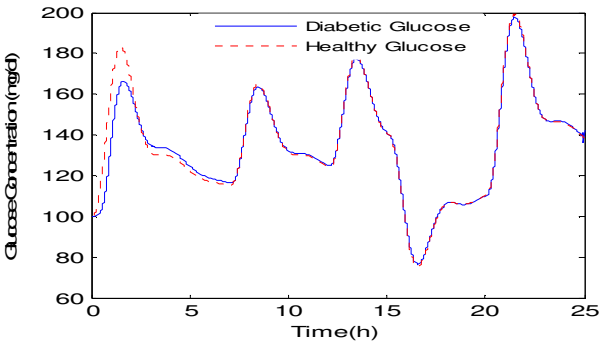


Figure.7. The outputs of the glucose concentration for a person in good health and a diabetic person for an initial value of 100 mg/dl for DMRAC control.

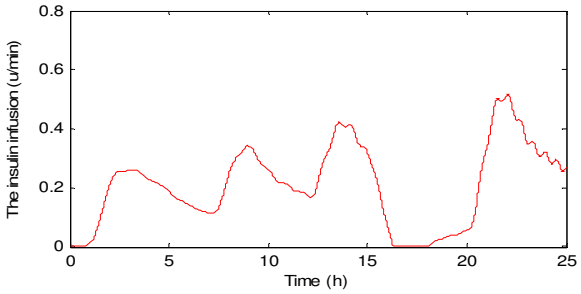


Figure.8. The control signal (the insulin infusion (u\min)).

### 5.3. Simulation Result with the MIT control on the Bergman Model

We considered the following values of systems parameters:

Table 2. The values considered for the simulation of the Bergman Model.

| The parameters | Normal Human | Patient 1 | Patient 2 |
|---|---|---|---|
| P1 | 0.0317 | 0.022 | 0.028 |
| P2 | 0.0123 | 0.0123 | 0.025 |
| P3 | $4.92\times10^{-6}$ | $6.92\times10^{-6}$ | 0.000005 |
| n | 0.2659 | 0.2660 | 0.2810 |
| Gb | 80 | 80 | 80 |
| Ib | 7 | 7 | 7 |

Simulation results of MIT control without disturbance are shown in Figure.9 to Figure.10. Then for direct model reference adaptive control in Figure.11 to Figure.12

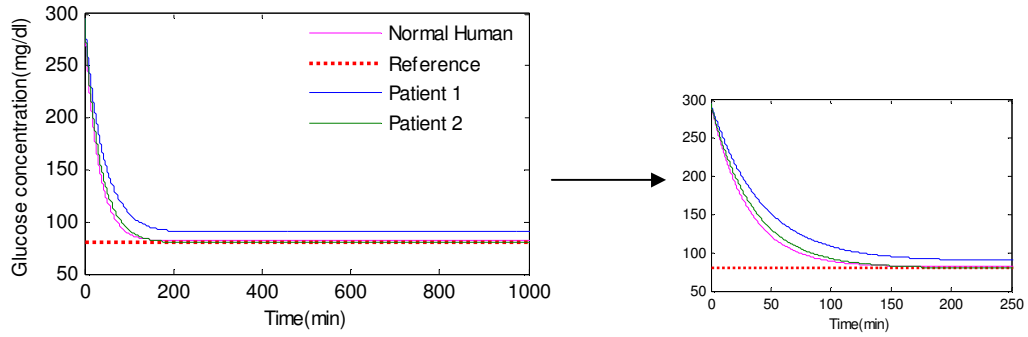


Figure. 9. The outputs of the glucose concentration of the MIT control for initial value $G_b$=300 (mg/dl).

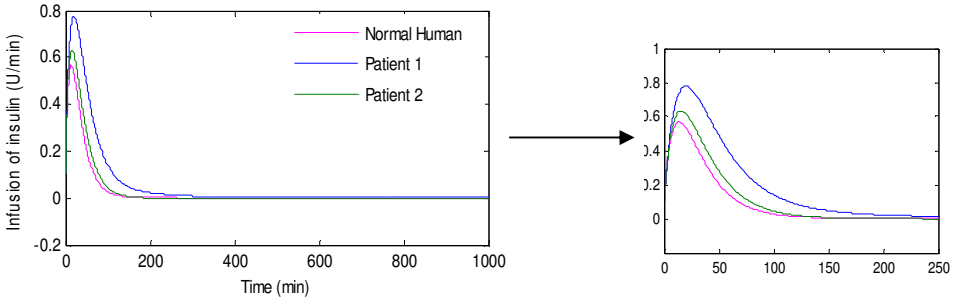


Figure.10. The insulin infusion (u\min) of the MIT control for initial value $G_b$=300(mg/dl).

## 5.4. Simulation Result with the DMRAC control on the Bergman Model

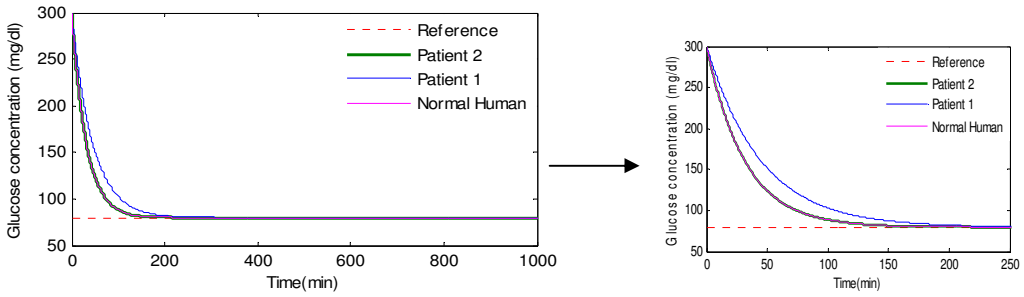


Figure. 11. The outputs of the glucose concentration of the DMRAC control for initial value $G_b$=300(mg/dl).

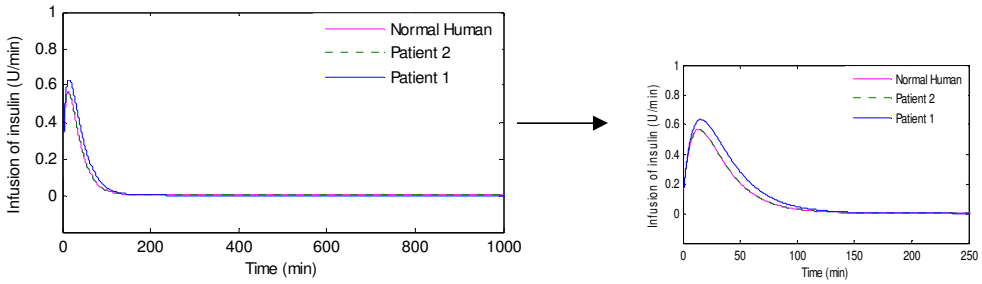


Figure.12. The insulin infusion (u\min) of the DMRAC control for initial value $G_b$=300(mg/dl)

According to the above simulation in Figures 9, 11 it is evident that the tracking of the glucose response for a diabetic person converge to the reference model. The glucose response of the diabetic person fluctuates. The convergence rate depends on the adaptation gain. It is important to get a reasonable value of this parameter.

From Figures.3,4 and Figures.6,7, for the Bolie model and Figures.9, 11 for the Bergman model, we can see that the convergence of glucose-insulin system output towards its reference, for the DMRAC controller is faster than the MIT controller, in general, we are more interested to the performances of the system in steady state, where we note that the use of the DMRAC is better than the MIT. Note that in Figure 3 and Figure 4, the adaptation of the glucose response of the diabetic to the healthy person is not smooth at time 0 to 5h.

## 6. CONCLUSIONS

In this paper, we have presented a treatment of continuous insulin infusion for diabetic patients from a control perspective. The Bolie and the Bergman Models is presented and discussed. Then an extension of model reference adaptive control based on DMRAC and MIT methods to the glucose-insulin system was developed. We conclude that the blood glucose concentration of a type 1 diabetic patient is stabilized at the desired level. The robustness of the two controllers has been confirmed through different parameters in patients. A simulation study has been presented to illustrate the effectiveness of the proposed controllers.

The applicability of adaptive controllers has now been extended to the non linear systems physiologies. Simulation results demonstrate the viability of the DMRAC and MIT algorithms designed.

Further works must be carried for an other models of glucose insulin system and an other controllers.

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