

Variational Iterational method for solving IVGTT glucose-insulin model with two distributed delays

K.Krishnan ^{*1} and M.C. Maheswari²

¹*Research Department of Mathematics, Cardamom Planters' Association College, Bodinayakanur-625 513, Tamilnadu, India.*

²*Department of Mathematics, V.V. Vanniyaperumal College for Women Virudhunagar-626 101, Tamilnadu, India.*

Abstract

In this paper, we investigate variational iteration method for solving distributed delay equations for system of glucose-insulin model. An algorithm based on He's variational iteration method (VIM) is developed to approximate the solution of a non-linear mathematical model for glucose-insulin system. Using VIM, it is possible to find an exact solution or an approximate solution of the proposed model.

Key words: Glucose, Insulin, Distributed delays, State Systems, Variational Iteration Method.

Mathematics Subject Classification (2010): 37B25, 93C10, 93C23.

1. INTRODUCTION

All discrete and distributed delay differential equation models for IVGTT explicitly involve a time delay between the rise in glycemia and the correspondingly stimulated insulin secretion. Observable delay effects are often gradual (distributed) and smooth in most physiological systems, it is thus natural to utilize distributed delay parameters rather than discrete. Some authors proposed the IVGTT glucose insulin model with distributed delays [1,2]. All IVGTT models in [1,3,4] follow the same criterion, which yields a value of around 20 min. It is well known that a large delay can destabilize a system. An accurate assessment of the delay can therefore play a critical role in elucidation of the metabolic portrait.

An effective method is required to analyze the mathematical model which provides solutions conforming to physical reality. Therefore, we must be able to solve nonlinear delay differential equations. Common analytic procedures linearize the

system or assume that nonlinearities are relatively insignificant. Such procedures change the actual problem to make it tractable by the conventional methods. In short, the physical problem is transformed to a purely mathematical one, for which the solution is readily available. Recently, several numerical and approximate methods to solve the differential equations have been given such as variational iteration method [5], homotopy perturbation method [6], A domain decomposition method, homotopy analysis method and collocation method (see) [7, 8]. Among them of these methods is the variational iteration method which is proposed by He [5] as a modification of the general Lagrange multiplier method. This method is based on the use of restricted variations and correction functional which has found a wide application for the solution of non-linear differential equations [9]. This method does not require the presence of small parameters in the differential equation, and does not require that the nonlinearities be differentiable with respect to the dependent variable and its derivatives. This technique provides a sequence of functions which converges to the exact solution of the problem. He's variational iteration method (VIM) gives the new direction of research and its application might go more inside into the modeling of the dynamical system. In this paper, an algorithm based on He's VIM is developed to approximate the solution of a nonlinear mathematical model of glucose insulin dynamics. The organization of the paper is as follows: In section 2, we describe the model for glucose-insulin system. We review and the application of VIM in section 3, Finally ends with conclusion in section 4.

2. MODEL DESCRIPTION

An analytic methodology is introduced in order to recast the distributed-delay nonlinear models into a nonlinear systems without delay, in front of an increase of the state space dimension. The availability of real-time data on the insulin concentration is a prerequisite for the development of an artificial pancreas controlling in real time the blood glucose level with optimum insulin infusions from an in vivo pump [2]. They dealt with the problem of the state reconstruction, by applying the theory of asymptotic state observation for nonlinear model systems, has been explored for distributed-delay kernel models of glucose- insulin homeostasis

without Michaelis-Menten $\frac{G(t)}{\alpha G(t)+1}$ this section is developed to present a family of

double kernel disrupted – delay differential models for the glucose-insulin homeostasis, we begin with the model as follows:

$$\begin{aligned} \frac{dG(t)}{dt} &= -b_1 G(t) - \frac{b_4 G(t)}{\alpha G(t)+1} \int_0^{\infty} w_1(s) I(t-s) ds + b_7 \\ \frac{dI(t)}{dt} &= -b_2 I(t) - b_6 \int_0^{\infty} w_G(s) G(t-s) ds \end{aligned} \quad (2.1)$$

With initial conditions

$$\begin{aligned}
 G(t) &\equiv G_b \forall t \in (-\infty, 0), & G(0) &= G_b + b_0 \\
 I(t) &\equiv I_b \forall t \in (-\infty, 0), & I(0) &= G_b + b_3 b_0
 \end{aligned}
 \tag{2.2}$$

Note that a subscript has been added to the weighting functions ω to distinguish between glucose and insulin kinetics. The delay kernel is also present, where the first kernel $I(t - s)$ must be considered for a change in insulin concentration to affect plasma glucose production, the second kernel $G(t-s)$ denote the delay before the pancreas can be respond to change in blood glucose. We assume instead that the insulin-dependent net glucose tissue uptake takes the more general and realistic michaleelis-Menten form $\frac{G(t)}{\alpha G(t)+1}$ which has maximum capacity $\frac{b_4}{\alpha}$. The parameter α , in the response function $\frac{G(t)}{\alpha G(t)+1}$ is non -negative $\frac{1}{\alpha}$ is the half-saturation constant. The reason for this is simply due to the limit of time and the capacity of insulin's ability of digesting glucose.

The weight function $\omega(t)$ is a non-negative square integrable function defined on $\mathbb{R}^+ = [0, \infty)$ such that

$$\int_0^\infty \omega(t) dt = 1, \quad \int_0^\infty t\omega(t) dt < +\infty
 \tag{2.3}$$

The finite equality $\Delta_a = \int_0^\infty t\omega(t) dt < +\infty$ has the meaning of an average time delay.

The properties of the two kernels ωI and $\omega I t$ are similar; in particular conditions (2.3), are both true. In this work the assumption that $\omega I t(t) \equiv \omega I(t) \equiv \omega(t)$ as considered, that means $\gamma I = \gamma I t = \gamma$, according to our model (2.1). By introducing the following further state components as follows:

$$\begin{aligned}
 \eta G(t) &= \int_0^\infty \omega(s) I(t-s) ds \\
 \xi G(t) &= \int_0^\infty e^{-\gamma(t-s)} I(s) ds \\
 \eta I(t) &= \int_0^\infty \omega(s) G(t-s) ds
 \end{aligned}$$

$$\xi I(t) = \int_0^{\infty} e^{-\gamma(t-s)} G(s) ds \quad (2.4)$$

In order to solve the state estimation problem, a first order differential system has to be achieved from (2.1). The following nonlinear system is obtained from (2.1),

$$\begin{aligned} \dot{x}_1(t) &= -b_1 x_1(t) - \frac{b_4 x_1(t) x_3(t)}{\alpha x_1(t) + 1} + b_7 \\ \dot{x}_2(t) &= -b_2 x_2(t) + b_6 x_5(t) \\ \dot{x}_3(t) &= -\gamma x_3(t) + \gamma^2 x_4(t) \\ \dot{x}_4(t) &= -\gamma x_4(t) + x_2(t) \\ \dot{x}_5(t) &= -\gamma x_5(t) + \gamma^2 x_6(t) \\ \dot{x}_6(t) &= -\gamma x_6(t) + x_1(t) \end{aligned} \quad (2.5)$$

This approach to the numerical quantification of the homeostasis of the glucose insulin system from the mathematical modeling of the IVGTT has the advantage of explicitly representing the two arms of the whole system together (insulin sensitivity of tissues and pancreatic sensitivity to circulating glucose), allowing the eventual simultaneous fitting of glucose and insulin concentration data. Parameters are described in Table I and their values are taken from [10].

Parameters description for Glucose-Insulin model

Parameters	Units	Biological Description
b_0	mg/dl	Theoretical increase in plasma concentration over basal glucose concentration at time zero after instantaneous administration and redistribution of the I.V. glucose bolus
b_1	min^{-1}	Spontaneous glucose first order disappearance rate constant
b_2	min^{-1}	The apparent first order disappearance rate for insulin
b_3	$pM/(mg/dl)$	The first-phase insulin concentration increase, increase in the concentration of glucose at time zero due to the injected bolus

b_4	$\text{min}^{-1}pM^{-1}$	The constant amount of insulin-dependent glucose disappearance rate of plasma insulin concentration
b_6	$\text{min}^{-1}pM/(\text{mg/dl})$	The constant amount of second-phase insulin release rate of average plasma glucose concentration per unit time
b_7	$(\text{mg/dl})\text{min}^{-1}$	The constant increase in plasma glucose concentration due to to the constant baseline liver glucose

3. Variational Iteration Method

The VIM method has been employed to solve a large variety of linear and nonlinear problems with approximations converging rapidly to accurate solutions. Some advantages of this technique are

1. The initial condition can be chosen freely with some unknown parameters
2. The unknown parameters in the initial condition can be easily identified.
3. The calculation is simple and straightforward.

This approach is successfully and effectively applied to various equations, see for example [5, 11, 12].

The VIM transforms the differential equation to a recurrence sequence of functions and the limit of the sequence, if exists, is considered as the solution of the differential equation. Consider the following differential equation

$$Lu(t) + Mu(t) = g(t) \tag{3.6}$$

where L is a linear operator, M is a known analytic function, r_i is the delay term and $g(t)$ is an inhomogeneous term. Given an initial guess $u_0(t)$, a correctional functional as

$$u_{n+1}(t) = u_n(t) + \int_0^t \lambda(\xi)(Lu_n(\xi) + M\tilde{u}_n(\xi) - g(\xi))d\xi, n \geq 1 \tag{3.7}$$

is made, where λ is a general Lagrangian multiplier [5, 11] which can be identified optimally via the variational theory and the function \tilde{u}_n is a restricted variation which means $\delta\tilde{u}_n = 0$. After determining the Lagrange multiplier λ and selecting an appropriate initial function u_0 , the successive approximation u_n of the solution can be readily obtained [12]. Consequently, the exact solution may be obtained by using

$$u = \lim_{n \rightarrow \infty} u_n$$

Now, to illustrate how to find the value of the Lagrange multiplier λ , we will consider the following case, which is dependent on the order of the operator L in

(3.6), we will study the case operator $L = \frac{d}{dt}$ (without loss of generality)

Making the above correction functional stationary, and noticing that $\delta\tilde{u}_n = 0$ we obtain

$$\delta u_{n+1}(t) = \delta u_{n+1}(t) + \int_0^t \lambda(\xi)(Lu_n(\xi) + M\tilde{u}_n(\xi) - g(\xi))d\xi,$$

$$\delta u_{n+1}(t) = \delta u_{n-1}(t) + \lambda(\xi)\delta u_{n-1}\Big|_{\xi=t} - \int_0^t \lambda'(\xi)[\delta u_{n-1}]d\xi = 0,$$

where $\delta\tilde{u}_n$ is considered as a restricted variation i.e., $\delta\tilde{u}_n = 0$, yields the following stationary conditions

$$\lambda'(\xi) = 0, \quad 1 + \lambda(\xi)\Big|_{\xi=t} = 0 \quad (3.8)$$

This equation is known as Lagrange - Euler equation with natural boundary condition. The solution of this equation gives the Lagrange multiplier $\lambda(\xi) = -1$. Now, the following variational iteration formula can be obtained

$$u_{n+1}(t) = u_n(t) - \int_0^t (Lu_n(\xi) + M\tilde{u}_n(\xi) - g(\xi))d\xi, \quad (3.9)$$

We start with an initial approximation, and by using the above iteration formula (3.9), we can obtain directly the other components of the solution. The several approximations $u_n(t)$, $n \geq 0$, follow immediately, the exact solution may be obtained by using

$$u(t) = \lim_{n \rightarrow \infty} u_n(t).$$

3.1 Application of VIM

The VIM is useful to obtain exact and approximate solutions for linear and nonlinear delay differential equations. It has been used to solve effectively, easily and accurately a large class of nonlinear problems with approximations. To show the efficiency of the VIM method, in this subsection, we apply the VIM to solve the following system of nonlinear ordinary differential equation (2.5).

According to the VIM, we can construct the correction functional as follows:

$$x_{1,n+1}(t) = x_{1,n}(t) + \int_0^t \lambda_1(\xi)[x'_{1,n}(\xi) + \frac{b_4 x_{1,n}(\xi) x_{3,n}(\xi)}{\alpha x_{1,n}(\xi) + 1} - b_7]d\xi,$$

$$\begin{aligned}
 x_{2,n+1}(t) &= x_{2,n}(t) + \int_0^t \lambda_2(\xi) [x'_{2,n}(\xi) + b_2 x_{2,n}(\xi) - b_6 \tilde{x}_{5,n}(\xi)] d\xi, \\
 x_{3,n+1}(t) &= x_{3,n}(t) + \int_0^t \lambda_3(\xi) [x'_{3,n}(\xi) + \gamma x_{3,n}(\xi) - \gamma^2 \tilde{x}_{4,n}(\xi)] d\xi, \\
 x_{4,n+1}(t) &= x_{4,n}(t) + \int_0^t \lambda_4(\xi) [x'_{4,n}(\xi) + \gamma x_{4,n}(\xi) - \tilde{x}_{2,n}(\xi)] d\xi, \\
 x_{5,n+1}(t) &= x_{5,n}(t) + \int_0^t \lambda_5(\xi) [x'_{5,n}(\xi) + \gamma x_{5,n}(\xi) - \gamma^2 \tilde{x}_{6,n}(\xi)] d\xi, \\
 x_{6,n+1}(t) &= x_{6,n}(t) + \int_0^t \lambda_6(\xi) [x'_{6,n}(\xi) + \gamma x_{6,n}(\xi) - \tilde{x}_{1,n}(\xi)] d\xi. \tag{3.10}
 \end{aligned}$$

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ and λ_6 are the general Lagrange multipliers, and $\tilde{x}_{1,n}, \tilde{x}_{2,n}, \tilde{x}_{3,n}, \tilde{x}_{4,n}, \tilde{x}_{5,n}$ and $\tilde{x}_{6,n}$ denote restricted variations, i.e., $\delta \tilde{x}_{1,n} = \delta \tilde{x}_{2,n} = \delta \tilde{x}_{3,n} = \delta \tilde{x}_{4,n} = \delta \tilde{x}_{5,n} = \delta \tilde{x}_{6,n} = 0$. Making the above correction functional stationary as,

$$\begin{aligned}
 \delta x_{1,n+1}(t) &= \delta x_{1,n}(t) + \delta \int_0^t \lambda_1(\xi) [x'_{1,n}(\xi) + b_1 x_{1,n}(\xi)] d\xi, \\
 &= \delta x_{1,n}(t) + \delta \lambda_1(\xi) x_{1,n}(\xi) |_{\xi=t} + \delta \int_0^t [b_1 \lambda_1(\xi) - \lambda'_1(\xi)] x_{1,n}(\xi) d\xi = 0 \tag{3.11}
 \end{aligned}$$

$$\begin{aligned}
 \delta x_{2,n+1}(t) &= \delta x_{2,n}(t) + \delta \int_0^t \lambda_2(\xi) [x'_{2,n}(\xi) + b_2 x_{2,n}(\xi)] d\xi, \\
 &= \delta x_{2,n}(t) + \delta \lambda_2(\xi) x_{2,n}(\xi) |_{\xi=t} + \delta \int_0^t [b_2 \lambda_2(\xi) - \lambda'_2(\xi)] x_{2,n}(\xi) d\xi = 0 \tag{3.12}
 \end{aligned}$$

$$\begin{aligned}
 \delta x_{3,n+1}(t) &= \delta x_{3,n}(t) + \delta \int_0^t \lambda_3(\xi) [x'_{3,n}(\xi) + \gamma x_{3,n}(\xi)] d\xi, \\
 &= \delta x_{3,n}(t) + \delta \lambda_3(\xi) x_{3,n}(\xi) |_{\xi=t} + \delta \int_0^t [\gamma \lambda_3(\xi) - \lambda'_3(\xi)] x_{3,n}(\xi) d\xi = 0 \tag{3.13}
 \end{aligned}$$

$$\begin{aligned}\delta x_{4,n+1}(t) &= \delta x_{4,n}(t) + \delta \int_0^t \lambda_4(\xi) [x'_{4,n}(\xi) + \gamma x_{4,n}(\xi)] d\xi, \\ &= \delta x_{4,n}(t) + \delta \lambda_4(\xi) x_{4,n}(\xi) \Big|_{\xi=t} + \delta \int_0^t [\gamma \lambda_4(\xi) - \lambda'_4(\xi)] x_{4,n}(\xi) d\xi = 0\end{aligned}\quad (3.14)$$

$$\begin{aligned}\delta x_{5,n+1}(t) &= \delta x_{5,n}(t) + \delta \int_0^t \lambda_5(\xi) [x'_{5,n}(\xi) + \gamma x_{5,n}(\xi)] d\xi, \\ &= \delta x_{5,n}(t) + \delta \lambda_5(\xi) x_{5,n}(\xi) \Big|_{\xi=t} + \delta \int_0^t [\gamma \lambda_5(\xi) - \lambda'_5(\xi)] x_{5,n}(\xi) d\xi = 0\end{aligned}\quad (3.15)$$

and

$$\begin{aligned}\delta x_{6,n+1}(t) &= \delta x_{6,n}(t) + \delta \int_0^t \lambda_6(\xi) [x'_{6,n}(\xi) + \gamma x_{6,n}(\xi)] d\xi, \\ &= \delta x_{6,n}(t) + \delta \lambda_6(\xi) x_{6,n}(\xi) \Big|_{\xi=t} + \delta \int_0^t [\gamma \lambda_6(\xi) - \lambda'_6(\xi)] x_{6,n}(\xi) d\xi = 0\end{aligned}\quad (3.16)$$

The equations (3.11), (3.12), (3.13), (3.14), (3.15) and (3.16) yield the following stationary conditions,

$$\begin{aligned}\lambda'_1(\xi) - b_1 \lambda_1(\xi) &= 0, & 1 + \lambda_1(\xi) \Big|_{\xi=t} &= 0, \\ \lambda'_2(\xi) - b_2 \lambda_2(\xi) &= 0, & 1 + \lambda_2(\xi) \Big|_{\xi=t} &= 0, \\ \lambda'_3(\xi) - \gamma \lambda_3(\xi) &= 0, & 1 + \lambda_3(\xi) \Big|_{\xi=t} &= 0, \\ \lambda'_4(\xi) - \gamma \lambda_4(\xi) &= 0, & 1 + \lambda_4(\xi) \Big|_{\xi=t} &= 0, \\ \lambda'_5(\xi) - \gamma \lambda_5(\xi) &= 0, & 1 + \lambda_5(\xi) \Big|_{\xi=t} &= 0, \\ \lambda'_6(\xi) - \gamma \lambda_6(\xi) &= 0, & 1 + \lambda_6(\xi) \Big|_{\xi=t} &= 0.\end{aligned}\quad (3.17)$$

The general Lagrange multipliers can be identified by solving the system of equations in (3.17), to obtain $\lambda_1(\xi) = -e^{b_1(\xi-t)}$, $\lambda_2(\xi) = -e^{b_2(\xi-t)}$, $\lambda_3(\xi) = -e^{\gamma(\xi-t)}$, $\lambda_4(\xi) = -e^{\gamma(\xi-t)}$, $\lambda_5(\xi) = -e^{\gamma(\xi-t)}$, $\lambda_6(\xi) = -e^{\gamma(\xi-t)}$.

$$x_{1,n+1}(t) = x_{1,n}(t) - \int_0^t e^{b_1(\xi-t)} \left[x'_{1,n}(\xi) + b_1 x_{1,n}(\xi) + \frac{b_4 x_{1,n}(\xi) \tilde{x}_{3,n}(\xi)}{\alpha x_{1,n}(\xi) + 1} - b_7 \right] d\xi,$$

$$\begin{aligned}
 x_{2,n+1}(t) &= x_{2,n}(t) - \int_0^t e^{b_2(\xi-t)} \left[x'_{2,n}(\xi) + b_2 x_{2,n}(\xi) - b_6 \tilde{x}_{5,n}(\xi) \right] d\xi, \\
 x_{4,n+1}(t) &= x_{4,n}(t) \int_0^t e^{\gamma(\xi-t)} \left[x'_{4,n}(\xi) + \gamma x_{4,n}(\xi) - \tilde{x}_{2,n}(\xi) \right] d\xi, \\
 x_{5,n+1}(t) &= x_{5,n}(t) \int_0^t e^{\gamma(\xi-t)} \left[x'_{5,n}(\xi) + \gamma x_{5,n}(\xi) - \gamma^2 \tilde{x}_{6,n}(\xi) \right] d\xi, \\
 x_{6,n+1}(t) &= x_{6,n}(t) - \int_0^t e^{\gamma(\xi-t)} \left[x'_{6,n}(\xi) + \gamma x_{6,n}(\xi) - \tilde{x}_{1,n}(\xi) \right] d\xi. \quad (3.18)
 \end{aligned}$$

We start with initial approximations $x_1(0)$, $x_2(0)$, $x_3(0)$, $x_4(0)$, $x_5(0)$, $x_6(0)$. We obtained the value of $x_{1,n+1}(t)$, from the first equation of (3.18), the value of $x_{2,n+1}(t)$ from the second equation of (3.18), the value of $x_{3,n+1}(t)$ from the third equation of (3.18), the value of $x_{4,n+1}(t)$ from the fourth equation of (3.18), the value of $x_{5,n+1}(t)$ from the fifth equation of (3.18) and the value of $x_{6,n+1}(t)$ from the sixth equation of (3.18), this increases the convergence rate. By the above iteration formula (3.18), we can obtain a few first terms being calculated.

$$x_{1,1}(t) = 78.9684059 + 241.0315941 \left(1 - 0.509t + \frac{0.0509^2 t^2}{2!} + \frac{0.0509^3 t^3}{3!} + \frac{0.0509^4 t^4}{4!} + \frac{0.0509^5 t^5}{5!} \right) + o(h^6), \quad (3.19)$$

$$x_{2,1}(t) = 51.7216295 + 855.5283705 \left(1 - 0.2062t + \frac{0.2062^2 t^2}{2!} + \frac{0.2062^3 t^3}{3!} + \frac{0.2062^4 t^4}{4!} + \frac{0.2062^5 t^5}{5!} \right) + o(h^6), \quad (3.20)$$

$$x_{3,1}(t) = 5.17000000 + 46.53000000 \left(1 - 0.02t + \frac{0.02^2 t^2}{2!} + \frac{0.02^3 t^3}{3!} + \frac{0.02^4 t^4}{4!} + \frac{0.02^5 t^5}{5!} \right) + o(h^6), \quad (3.21)$$

$$x_{4,1}(t) = 45362.5 - 45104 \left(1 - 0.02t + \frac{0.02^2 t^2}{2!} + \frac{0.02^3 t^3}{3!} + \frac{0.02^4 t^4}{4!} + \frac{0.02^5 t^5}{5!} \right) + o(h^6), \quad (3.22)$$

$$x_{5,1}(t) = 7.90000000 + 71.10000000 \left(1 - 0.02t + \frac{0.02^2 t^2}{2!} + \frac{0.02^3 t^3}{3!} + \frac{0.02^4 t^4}{4!} + \frac{0.02^5 t^5}{5!} \right) + o(h^6), \quad (3.23)$$

$$x_{6,1}(t) = 16000.00 - 15605.00 \left(1 - 0.02t + \frac{0.02^2 t^2}{2!} + \frac{0.02^3 t^3}{3!} + \frac{0.02^4 t^4}{4!} + \frac{0.02^5 t^5}{5!} \right) + o(h^6), \quad (3.24)$$

While,

$$x_{1,2}(t) = 320.0000000 - 12.26850814t + 0.3122335322t^2 + 0.000431801667t$$

$$\left\{ -4X10^{-8} \left(\frac{(-1 - 7237.05t + 294.0937500t^2 - 6.526356100t^3 + 0.04685352968t^4)}{21 - 0.6134254070t + 0.01561167661t^2} \right)^3 \right\}$$

$$- 0.02545t \left\{ -4X10^{-8} \left(\frac{(-1 - 7237.05t + 294.0937500t^2 - 6.526356100t^3 + 0.04685352968t^4)}{21 - 0.6134254070t + 0.01561167661t^2} \right)^2 \right\}$$

$$+ t \left\{ -4X10^{-8} \left(\frac{(-1 - 7237.05t + 294.0937500t^2 - 6.526356100t^3 + 0.04685352968t^4)}{21 - 0.6134254070t + 0.01561167661t^2} \right)^3 \right\}$$

$$x_{2,2}(t) = 907.2500000 - 176.4099500t + 17.99589584t^2 - 0.001558298661t^4$$

$$+ 0.00001360378195t^5 + 0.02171180800t^3,$$

$$x_{3,2}(t) = 51.70000000 - 0.9306000000t + 0.3701380000t^2 - 0.00001202773334t^4$$

$$- 2.405546666X10^{-7}t^5,$$

$$x_{4,2}(t) = 258.5 + 902.08t - 185.4307500t^2 + 0.1701179951t^4 + 16.42376634t^3$$

$$+ 0.001212524390t^5,$$

$$x_{5,2}(t) = 79.00000000 - 1.422000000t + 0.01422000000t^2 - 0.0000666666667t$$

$$(.1248400000 - 0.001248400000t^2)^3 + 0.01t(.1248400000t - 0.001248400000t^2)^2$$

$$+ t(.1248400000t - 0.001248400000t^2),$$

$$x_{6,2}(t) = 395.00 + 312.1000t - 3.121t^2 - 0.00006666666667t(12.26850814t - .3122335322t^2)^3 \\ - 0.01t(12.26850814t - .3122335322t^2)^2 - t(12.26850814t - .3122335322t^2)$$

Continuing in this manner, the rest of components of the iteration formulas can be obtained using symbolic packages such as Maple. In our case, only two terms of the iteration values are given.

4 DISCUSSION

In the present work, we have investigated a model of the glucose-insulin system for two different distributed delays. Throughout this paper, the He's variational iteration method has been successfully applied to find the approximate solution of nonlinear delay differential equations. We can find that VIM method is extremely efficient to solve this biological model. From the solutions obtained using the suggested method we can conclude that these solutions are in excellent agreement with the exact solution and show that these approaches can solve the problem effectively.

REFERENCES

- [1] A. Mukhopadhyay, A. De Gaetano, O. Arino, Modelling the intra-venous glucose tolerance test: a global study for a single distributed delay model, *Dis. and Contin. Dyn. Syst. - Series B*, 4(2): 407-417, (2004).
- [2] A. De Gaetano, D. Di Martino, A. Germani, C. Manes, P. Palumbo, Distributed delay models of the glucose-insulin homeostasis and asymptotic state observation *Istituto Di Analisi Dei Sistemi Ed Informatica Consiglio Nazionale Delle Ricerche*, R.618, (2004).
- [3] Li, Y. Kuang, B. Li, Analysis of IVGTT glucose - insulin interaction models with time-delay, *Dis. and Contin. Dyn. Syst. - Series B*, 1 (1): 103-124, 2001.
- [4] D.V.Giang, Y. Lenbury, A. De Gaetano, P. Palumbo, Delay model of glucose - insulin systems: global stability and oscillated solutions conditional on delays, *J. Math. Anal. Appl.*, 343(2)-996, (2008).
- [5] J. H. He Variational iteration method-a kind of nonlinear analytical technique: some examples. *Int. J. Nonlinear Mech.* 34, 699 - 708 (1999)
- [6] N.H. Sweilam, M.M. Khader, and R.F. Al-Bar Numerical studies for a multi order fractional differential equation *Physics Letters A*, 371, 26-33, (2007).
- [7] M. M. Khader On the numerical solutions for the fractional diffusion equation *Physics Letters A* 16, 2535-2542, (2011).

- [8] N.H. Sweilam and M.M. Khader Numerical studies for fractional-order Logistic differential equation with two different delays *J. Appl. Math.*, 2012, pp-14, (2012) .
- [9] N.H. Sweilam and M.M. Khader On the convergence of VIM for nonlinear coupled system of partial differential equations *Int. J. of Computer Maths.*, 87(5), 1120-1130, (2010).
- [10] De Gaetano A, Arino O Mathematical modeling of the intravenous glucose tolerance test. *Journal of Mathematical Biology.* 40 (2), 136 - 168 (2000)
- [11] J. H. He Variational iteration method for autonomous ordinary differential systems. *Appl. Math. Comput.* 114, 115 - 123 (2000)
- [12] Tatari M, Dehghan M On the convergence of He's variational iteration method. *J. Comput. Appl. Math.* 207, 121 - 128 (2007)