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Perturbation Iteration Method Compared with Direct Method and Fuzzy Logic Strategy for Solving An Optimal Control Problem of An Uninfected Hepatitis B Virus Dynamics

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Abstract

This paper aims at solving the optimal control problem of the dynamic of HBV infection under treatment using the perturbation iteration method. This method serves as a tool to determine the approximate solutions of nonlinear equations for which exact solutions cannot be obtained. To test the efficacy of this method, the authors propose to compare the numerical simulation results with those of the direct method and fuzzy logic strategy. The newly used method for solving the above optimal control problem is very important since the findings compared to those obtained from the two other methods are in good agreement with experimental data and they demonstrate the response drugs to the dynamics of uninfected hepatocytes, infected hepatocytes, and free virions for a patient suffering from HBV. Since the perturbation iteration method provides satisfactory results which are close to other used numerical methods, it is an important numerical tool to determine the solution of an optimal control problem. In particular, it provides optimal trajectories in medicine, biology, and other related scientific fields. For instance, the response of treatment as control of the human body ensures the health of patients.

Keywords: perturbation iteration; direct fuzzy logic; optimal control; HBV; numerical simulation.

1 Introduction

One of the major global public health concerns is Hepatitis [35]. It is a liver infection whose contact with infected blood or infected fluids of the individual body is the mode of transmission. Hepatitis B virus (HBV) damages the liver through acute hepatitis B infection and chronic hepatitis B infection [19]. The difference between them is that the first lasts less than six months whereas the second lasts six months or longer. In addition, the role of the patient's immune system suffering from acute hepatitis B infection is to clear the virus from the body so that he/she should recover completely within a few months. It is important to note that at birth, most infants infected with HBV manifest chronic hepatitis B infection, and many children are infected if they age between 1 and 6 years. Furthermore, around 80-90% of infants can be infected in the first year of life while in the first 5 years of life 30-50% of children infected develop chronic infection. This does not happen for adults since there is only 5% infected later in life [32]. Genetically, the genotype mutants occur naturally and the level of serum deoxyribonucleic acid is the identified factor that influences HBV progression. The replication process of HBV is done in the machinery of infected hepatocyte cells. The hepatitis B virion can bind to these cells through molecular structures on the surface of viruses (Antigen). The virus is engulfed using the endocytosis process. Once the infection occurs, the body's immune system starts attacking infected hepatocytes to clean the virus. This mechanism leads to liver injury since it is damaged by an adaptive immune response, particularly the virus-specific cytotoxic T lymphocytes (CTLs) which kill the cells that contain the virus. The antigen-nonspecific inflammatory aggravates the liver damage and the platelets are activated at the site of infection. Long-term consequences of chronic HBV infection are principally cirrhosis and cancer such as hepatocellular carcinoma (HCC) [15, 32] which attacks more than half of patients worldwide.

In 2015, there were 887,000 deaths due to HBV-related liver disease among 257 million HBV carriers in the world [28]. In addition, one in four people chronically infected people are at risk of premature death from cirrhosis or liver cancer [5]. The results of the research show that there is the impact of epidemic diseases on patients suffering from HBV which is a chronic disease [8, 11]. The way to reduce the number of HBV infections is to establish a vaccination program, which is the bats and the cheapest to prevent this liver disease. If it is well implemented, the incidence rates of childhood HCC are reduced. However, to prevent the replication of HBVs, hepatitis antiviral drugs are used. They save the liver from cirrhosis and cancer if they are well administrated. The drugs used to treat chronic HBV are of different types. These include adefovir dipivoxil, telbivudine, pegylated interferon, entecavir, alpha-interferon, lamivudine, telbivudine and tenofovir [33]. Mainly, the role of these drugs is to reduce the viral load so that the viral replication in the lever is decreased [24].

Mathematical models are an important source to support HBV dynamics and its treatment. They are useful tools to reveal emergent phenomena. The mathematical models enable extrapolation beyond scenarios that can be investigated because the knowledge base from the study and data can be greatly expanded throughout mathematical modeling which provides answers to questions otherwise, they are taken as unanswerable. Anderson and May used a simple mathematical model that shows the effects of carriers on the transmission of HBV [4]. The strategy to prevent HBV in New Zealand has been developed by Medley et al. using a mathematical model [25, 26] while an age structure model is proposed by Zhao et al. to predict the dynamics of HBV transmission and evaluate the long-term effectiveness of the vaccination program in China [36]. The control measures and the impact of vaccination on HBV infection have been explored by Pang et al. throughout their developed mathematical model [30]. The development of optimal therapeutic strategies for biomedical problems should be based on control theory. Taking a treatment regimen as a control variable to minimize the effects of a medical condition does this mechanism.

Moreover, the required drug doses of treatment for HBV-infected patients are determined using an optimal control theory [20, 33]. In this regard, Bhattacharyya and Ghosh [6], Kar and Batabyal [22], and Kar and Jana [23] developed an optimal control theory to solve biological problems. Particularly, the model predictive control (MPC) method is used to design an optimal treatment for HBV [16]. The delayed hepatitis B epidemic model based on stochastic analysis is developed by Din Anwarud et al.[12].

In addition, Din Anwarud developed a mathematical model for controlling COVID-19 which has effects on HBV patients [11]. The factors influencing HBV have been analyzed through the mathematical models developed by the same author in collaboration with co-workers [9, 14]. Using the epidemic model, Din Anwarud analyzed The stochastic bifurcation analysis and stochastic delayed optimal control [8]. The mathematical model can also be investigated using other methods. These include fractional order derivatives [7, 27]. The mathematical model equations can also be discretized using other base polynomials such as ones based upon Chebyshev polynomials or integrals [1, 21]. Recently, HBV has been the important focus of authors and researchers to capture the Caputo type fractional operator [10, 13].

This paper aims at the perturbation iteration method to solve the optimal control problem for investigating the dynamics of HBV. To test the efficacy of this method, numerical results are compared with those obtained using the direct method and an approach integrating fuzzy logic. Note that the optimal control problem involves the mathematical process of determining control and state trajectories for a dynamic system over a period of time to minimize a performance function. Different methods such as Caputo Fractional Derivative [17] and Four-Step Predictor-Corrector Method [31] can be used to solve this problem. One of them is the perturbation method. The advantage of this method is to determine the approximate solutions of nonlinear equations for which exact solutions cannot be obtained. In addition, the techniques of this method are useful for demonstrating, predicting, and describing phenomena in vibrating systems that are caused by nonlinear effects. Implemented using mathematical software such as Matlab, the direct method is a tool that can often provide solutions quickly and at a reduced time-consuming. This is an advantage of this method. Refer to [18] for the details of direct methods and approaches integrating fuzzy logic.

This paper focuses on describing the algorithm of the perturbation iteration method. The following is the structure of this paper. Section 2 deals with the model equations and optimal control problem. The description of the perturbation iteration method algorithm is in this section. Section 3 focuses on the application of the perturbation iteration method algorithm to solve an optimal control problem of HBV dynamics. Section 4 describes the numerical simulations while Section 5 presents concluding remarks.

2 Methods

2.1 Problem setting

The mathematical model equations we present have been proposed in [2] but Elaiw et al. incorporated the effect of two antivirals treatment for formulating an optimal control problem [16]. The model equations are as follows;

$$\frac{dT}{dt} = s - qT + aT\left[1 - \frac{T}{T_{\max}}\right] - \beta e^{-u_1}\frac{TV}{1+bV}, \tag{1}$$

$$\frac{dI}{dt} = \beta e^{-u_1} \frac{TV}{1+bV} - \delta I, \tag{2}$$

$$\frac{dV}{dt} = pe^{-u_2} I - cV, \tag{3}$$

where variables, parameters and particular functions are described in Table 1.

Table 1: Description of variable, parameters and particular chemotherapeutic functions.

Variable	**Description**
T (cells/dl)	Uninfected hepatocyte cells concentration
I (cells/dl)	Infected hepatocyte cells concentration
V (IU/ml)	Free virions concentration
Functions of chemotherapy	
e^{-u_1}	Chemotherapeutic function for preventing virus from infecting cells
e^{-u_2}	Chemotherapeutic function for preventing infected cells from producing the new viruses
Parameter	
s	Rate of production of uninfected hepatocytes
q	Rate of death rate of uninfected hepatocytes
a	The maximum rate of proliferation of target cells
$T_{\max}$	Maximum concentration of uninfected hepatocytes to shut off the proliferation
p	Rate of production of free virions from infected hepatocytes
β	Rate of infection to characterize infection efficiency
b	Positive constant of saturation functional response
δ	Rate of death of infected hepatocytes
c	Rate to clear viral particles

In (1)-(3), we set the state vector as $E = (T, I, V)^t$. The health of the patient is improved if his/her status is around the steady state $E_e = (T_e, 0, 0)^t$ where T_e is the concentration of uninfected hepatocytes of healthy subject. Furthermore, we can formulate the cost function in the following manner.

Find $u_1^*(t)$ and $u_2^*(t)$ solution of

$$\min_{u_1,u_2\in[0,1]} J(u_1, u_2) = \int_0^{T_f} q_T \left(T - T_0\right)^2 + q_u u_1(t)^2 + q_v u_2(t)^2, \tag{4}$$

subject to the system (1)-(3).

Thus, the solution of optimal control problem (4), equations (1)-(3) can be solved using different mathematical methods. In [18], the details about discretization, numerical solution of direct methods and approach integrating fuzzy logic are described. In this work, we focus on the perturbation iteration method. The goal is to compare the obtained results of the perturbation iteration method with ones obtained using direct methods and approach integrating fuzzy logic. This allows investigation of the efficacy of the perturbation iteration method.

2.2 Description of algorithm $PIA(1,m)$

Perturbation iteration method (PIM) is one of among known numerical methods developed in 2010 by Aksoy et al. [34]. After introducing correction terms of first derivatives, PIM combines perturbation expansions and Taylor series expansions of order one to produce an iteration scheme [3, 34]. Consequently, $PIA(1,1)$ denotes the algorithm of PIM. Although in this paper we implement $PIA(1,1)$ on (4), equations (1)-(3), PIM is described by discussing the general case $PIA(1,m)$ where correction terms in the Taylor series expansion is m.

Let us write vector state,

$$y=(y_1,y_2,...,y_K)^T,$$

and a system of ODEs of first order of the form,

$$\begin{cases} E_1\equiv(y_1,y_1,y_2,...,y_K,\varepsilon,t)=0,\\ E_2\equiv(y_2,y_1,y_2,...,y_K,\varepsilon,t)=0,\\ \qquad\vdots\\ E_K\equiv(y_k,y_1,y_2,...,y_K,\varepsilon,t)=0, \end{cases} \tag{5}$$

where ε denotes the perturbation parameter and t is the independent variable. Thus, the compact form of (5) is

$$E_k\equiv E_k\left(y_k,y_j,\varepsilon,t\right)=0,\qquad k=1,2,...,K,\qquad j=1,2,...,K, \tag{6}$$

and its approximate solution is

$$y_{k,n+1}=y_{k,n}+\varepsilon y_{k,n}^c, \tag{7}$$

where the approximate solution is given at order n. Around $\varepsilon=0$, Taylor series expansion of (6) becomes

$$E_k=\sum_{i=0}^{m}\frac{1}{i!}\left[\left(\frac{d}{d\varepsilon}\right)^i E_k\right]_{\varepsilon=0}\varepsilon^i,\qquad k=1,2,...,K, \tag{8}$$

where

$$\frac{d}{d\varepsilon}=\frac{\partial y_{k,n+1}}{\partial\varepsilon}\frac{\partial}{\partial y_{k,n+1}}+\left(\sum_{j=0}^{K}\frac{\partial y_{j,n+1}}{\partial\varepsilon}\frac{\partial}{\partial y_{j,n+1}}\right)+\frac{\partial}{\partial\varepsilon}. \tag{9}$$

Thus, iterative equation of order $(n+1)$ is

$$E_k\left(y_{k,n+1},y_{j,n+1},\varepsilon,t\right).$$

Hence, the first order differential equation becomes

$$E_k=\sum_{i=0}^{m}\frac{1}{i!}\left[\left(y_{k,n}^c\frac{\partial}{\partial y_{k,n+1}}+\left(\sum_{j=0}^{K}y_{j,n}^c\frac{\partial}{\partial y_{j,n+1}}\right)+\frac{\partial}{\partial\varepsilon}\right)^i E_k\right]_{\varepsilon=0}\varepsilon^i,\qquad k=1,2,...,K, \tag{10}$$

obtained after substituting (9) into (8). Note that to have an iteration solution of order $(n+1)$ we should solve (10).

Note that $PIA(1,m)$ can also be generalized to solve a system of ODEs for n correction terms. Then the algorithm would be $PIA(n,m)$. The details of this algorithm, can be found in [29]. This means that $PIA(1,m)$ is simple algorithm of the perturbation-iteration method. To implement this simple algorithm, we consider the following differential equation of order one

$$E(y,y,\varepsilon)=0, \tag{11}$$

where $y = y(t)$. Setting one term of correction in perturbation expansion, we obtain

$$y_{n+1} = y_n + \varepsilon y^c, \tag{12}$$

where we have taken iteration of order n, perturbation parameter ε and the correction term εy^c. Substituting (12) into (11) we get

$$E(y_n, y_n, 0) + \frac{\partial E(y, y, 0)}{\partial y}\varepsilon y^c + \frac{\partial E(y_n, y_n, 0)}{\partial y}\varepsilon y^c + \frac{\partial E(y_n, y_n, 0)}{\partial \varepsilon}\varepsilon = 0. \tag{13}$$

After reorganizing (13), we get

$$y^c + \frac{E_y}{E_y}y^c = -\frac{\varepsilon E_\varepsilon + E}{\varepsilon E_y}, \tag{14}$$

where at $\varepsilon = 0$ the derivatives calculated by setting $E_z = \dfrac{\partial E}{\partial z}$. Using integrating factor

$$\mu(t) = \exp\left(\int \frac{E_y}{E_y} dt\right),$$

the equation (14) becomes

$$\frac{d}{dt}\left(\mu(t) y^c\right) = \mu(t)\left(-\frac{\varepsilon E_\varepsilon + E}{\varepsilon E_y}\right),$$

so that,

$$\mu(t) y^c = -\int \mu(t)\left(\frac{\varepsilon E_\varepsilon + E}{\varepsilon E_y}\right) + C.$$

Hence,

$$y^c = \frac{C}{\mu(t)} - \frac{1}{\mu(t)}\int \mu(t)\left(\frac{\varepsilon E_\varepsilon + E}{\varepsilon E_y}\right), \tag{15}$$

$$= C\exp\left(-\int \frac{E_y}{E_y} dt\right) - \left[\int \left(\frac{\varepsilon E_\varepsilon + E}{\varepsilon E_y}\right)\exp\left(\int \frac{E_y}{E_y} dt\right)\right]\exp\left(-\int \frac{E_y}{E_y} dt\right). \tag{16}$$

Replacing (16) into (12), the iteration scheme yields,

$$ccly_{n+1} = y_n + \varepsilon C_n C \exp\left(-\int \frac{E_y(y_n, y_n, 0)}{E_y(y_n, y_n, 0)} dt\right) - \left[\int \left(\frac{\varepsilon E_\varepsilon(y_n, y_n, 0) + E(y_n, y_n, 0)}{\varepsilon E_y(y_n, y_n, 0)}\right)\right. \tag{17}$$

$$\left.\exp\left(\int \frac{E_y(y_n, y_n, 0)}{E_y(y_n, y_n, 0)} dt\right)\right]\exp\left(-\int \frac{E_y(y_n, y_n, 0)}{E_y(y_n, y_n, 0)} dt\right). \tag{18}$$

3 Implementation of Algorithm $PIA(1,1)$ on (4), (1)-(3)

To illustrate the algorithm $PIA(1,1)$, we consider a system of first-order differential equations in the following form:

$$\begin{cases} E\left(\dot{T}, T, I, V, \varepsilon\right) = \dot{T} - s + qT - \varepsilon aT\left[1 - \dfrac{T}{T_{\max}}\right] + \varepsilon\beta e^{-u_1}\dfrac{TV}{1+bV}, \\ G\left(T, \dot{I}, I, V, \varepsilon\right) = \dot{I} - \varepsilon\beta e^{-u_1}\dfrac{TV}{1+bV} + \delta I, \\ F\left(T, I, \dot{V}, V, \varepsilon\right) = \dot{V} - pe^{-u_2} I + cV. \end{cases}$$

In addition, we consider that:

$$\begin{cases} E = 0, \\ G = 0, \\ F = 0. \end{cases} \tag{19}$$

For $PIA(1,1)$, we set $y = (T, I, V)^t$ state vector and we take one correction term from the perturbation expansion,

$$y_{n+1} = y_n + \varepsilon y_n^c. \tag{20}$$

Taking $Y_y = \dfrac{dY}{dy}$ and substituting (20) into (19), then, expanding in a Taylor series gives,

$$\begin{cases} E\left(\dot{T}, T, I, V, 0\right) + E_T\left(\dot{T}, T, I, V, 0\right)\varepsilon T_n^c + E_{\dot{T}}\left(\dot{T}, T, I, V, 0\right)\varepsilon \dot{T}_n^c + \varepsilon E_\varepsilon = 0, \\ G\left(T, \dot{I}, I, V, 0\right) + G_I\left(T, \dot{I}, I, V, 0\right)\varepsilon I_n^c + G_{\dot{I}}\left(T, \dot{I}, I, V, 0\right)\varepsilon \dot{I}_n^c + \varepsilon G_\varepsilon = 0, \\ F\left(T, I, \dot{V}, V, 0\right) + F_V\left(T, I, \dot{V}, V, 0\right)\varepsilon V_n^c + F_{\dot{V}}\left(T, I, \dot{V}, V, 0\right)\varepsilon \dot{V}_n^c + \varepsilon V_\varepsilon = 0. \end{cases}$$

After calculation we obtain,

$$\begin{cases} \dot{T}_n - s + qT_n + \varepsilon q T_n^c + \varepsilon \dot{T}_n^c - \varepsilon a T_n\left[1 - \dfrac{T_n}{T_{\max}}\right] + \varepsilon \beta e^{-u_1}\dfrac{T_n V_n}{1 + bV_n} = 0, \\ \dot{I}_n + \delta I_n + \delta\varepsilon I_n^c + \varepsilon \dot{I}_n^c - \varepsilon \beta e^{-u_1}\dfrac{T_n V_n}{1 + bV_n} = 0, \\ \dot{V}_n - pe^{-u_2} I + V_n + c\varepsilon V_n^c + \varepsilon \dot{V}_n^c = 0, \end{cases}$$

that is

$$\begin{cases} \dot{T}_n^c + qT_n^c = \dfrac{-\dot{T}_n + s - qT_n}{\varepsilon} + aT_n\left[1 - \dfrac{T_n}{T_{\max}}\right] - \beta e^{-u_1}\dfrac{T_n V_n}{1 + bV_n}, \\ \dot{I}_n^c + \delta I_n^c = \dfrac{-\dot{I}_n - \delta I_n}{\varepsilon} + \beta e^{-u_1}\dfrac{T_n V_n}{1 + bV_n}, \\ \dot{V}_n^c + cV_n^c = \dfrac{-\dot{V}_n + pe^{-u_2} I_n - V_n}{\varepsilon}. \end{cases} \tag{21}$$

Thus, the matrix form of the system (21) becomes

$$Y_n^c = AY_n^c + M_\varepsilon, \tag{22}$$

where

$$A = \begin{pmatrix} q & 0 & 0 \\ 0 & \delta & 0 \\ 0 & 0 & c \end{pmatrix} \text{ and } M_\varepsilon = \begin{pmatrix} \dfrac{-\dot{T}_n + s - qT_n}{\varepsilon} + aT_n\left[1 - \dfrac{T_n}{T_{\max}}\right] - \beta e^{-u_1}\dfrac{T_n V_n}{1 + bV_n} \\ \dfrac{-\dot{I}_n - \delta I_n}{\varepsilon} + \beta e^{-u_1}\dfrac{T_n V_n}{1 + bV_n} \\ \dfrac{-\dot{V}_n + pe^{-u_2} I_n - V_n}{\varepsilon} \end{pmatrix}.$$

If $Q_{n_h}^c(t)$ denotes the fundamental matrix of homogeneous system (22), a particular solution $Y_{n_p}^c$ for this system is

$$Y_{n_p}^c(t) = Q_{n_h}^c(t)\int_{t_0}^{t}\left(Q_{n_h}^c(\tau)\right)^{-1} M_\varepsilon(\tau)\, d\tau, \tag{23}$$

and the general solution is

$$Y_n(t) = e^{A(t-t_0)}Y_n(0) + \int_{t_0}^{t} e^{A(t-\tau)}M_\varepsilon(\tau)d\tau, \tag{24}$$

$$= e^{A(t-t_0)}Y_n(0) + e^{At}\int_{t_0}^{t} e^{-A\tau}M_\varepsilon(\tau)d\tau, \tag{25}$$

where

$$e^{At} = Q^c_{n_h}(t)\Big(Q^c_{n_h}(0)\Big)^{-1}.$$

If $n = 0$, the fundamental matrix solution of homogeneous linear system (21) and its inverse are

$$Q^c_{0_h}(t) = \begin{pmatrix} e^{qt} & 0 & 0 \\ 0 & e^{\delta t} & 0 \\ 0 & 0 & e^{ct} \end{pmatrix} \text{ and } \Big[Q^c_{0_h}(t)\Big]^{-1} = \begin{pmatrix} e^{-qt} & 0 & 0 \\ 0 & e^{-\delta t} & 0 \\ 0 & 0 & e^{-ct} \end{pmatrix}.$$

Then $Q^c_{0_h}(0) = I_3$ (Identity matrix of order 3) and we have

$$e^{At} = \Big[Q^c_{0_h}(t)\Big]\Big[Q^c_{0_h}(0)\Big]^{-1} = Q^c_{0_h}(t).$$

Setting $M_\varepsilon = \Big(M_{1,\varepsilon}, M_{2,\varepsilon}, M_{3,\varepsilon}\Big)^t$, where

$$M_{1,\varepsilon}(t) = \frac{-\dot{T}_n + s - qT_n}{\varepsilon} + aT_n\left[1 - \frac{T_n}{T_{\max}}\right] - \beta e^{-u_1}\frac{T_nV_n}{1+bV_n},$$

$$M_{2,\varepsilon} = \frac{-\dot{I}_n - \delta I_n}{\varepsilon} + \beta e^{-u_1}\frac{T_nV_n}{1+bV_n},$$

and

$$M_{3,\varepsilon} = \frac{-\dot{V}_n + pe^{-u_2}I_n - V_n}{\varepsilon}.$$

We have

$$e^{-At}M_\varepsilon = \begin{pmatrix} e^{-qt}M_{1,\varepsilon} \\ e^{-\delta t}M_{2,\varepsilon} \\ e^{-ct}M_{3,\varepsilon} \end{pmatrix} \text{ and } \int_0^t e^{-At}M_\varepsilon = \begin{pmatrix} -\frac{1}{q}M_{1,\varepsilon}e^{-qt} \\ -\frac{1}{\delta}e^{-\delta t}M_{2,\varepsilon} \\ -\frac{1}{c}e^{-ct}M_{3,\varepsilon} \end{pmatrix}.$$

Hence,

$$ccly^c_{n_p}(t) = e^{At}\int_0^t e^{-At}M_\varepsilon, \tag{26}$$

$$= \begin{pmatrix} e^{qt} & 0 & 0 \\ 0 & e^{\delta t} & 0 \\ 0 & 0 & e^{ct} \end{pmatrix}\begin{pmatrix} -\frac{1}{q}M_{1,\varepsilon}e^{-qt} \\ -\frac{1}{\delta}M_{2,\varepsilon}e^{-\delta t} \\ -\frac{1}{c}M_{3,\varepsilon}e^{-ct} \end{pmatrix}, \tag{27}$$

$$= \begin{pmatrix} -\frac{1}{q}M_{1,\varepsilon} \\ -\frac{1}{\delta}M_{2,\varepsilon} \\ -\frac{1}{c}M_{3,\varepsilon} \end{pmatrix}. \tag{28}$$

In addition, we have

$$y_{nh} = e^{At} y_n(0) = \begin{pmatrix} e^{qt}T(0) \\ e^{\delta t}I(0) \\ e^{ct}V(0) \end{pmatrix}.$$

Finally, the successive iterations are given by

$$y_{n+1}(t) = y_{nh}(t) + \varepsilon y^c_{np}(t), \tag{29}$$

and the solution of optimal control problem (4), (1)-(3) is obtained if the cost function is minimized.

4 Numerical Simulation

The implementation in Matlab uses its built-in function "fmincon" which helps solve an optimal control problem such as (4) and (29). Since this function is used to minimize constrained cost functions. To obtain the solution we consider the parameters given in Table 2.

Table 2: The used parameters [18].

Parameter	a	q	s	δ	β	c	p	b	$T_{\max}$
Value	0.108	0.072	36	0.5	0.001	3	5	0.01	1500

In the numerical simulation, we consider the unhealthy subject with $T(0) = 200$ Cells/dl, $I(0) = 300$ Cells/dl and $V(0) = 500\ IU/mL$. The starting value of the controls u_1 and u_2 is 1 if treatment is absent and is 0 in the case of maximal use of therapy. To investigate the efficacy of the perturbation iteration method, the numerical results implemented using this method are compared with one calculated by the direct method and fuzzy logic strategy [18]. Figures 1 and 2 illustrate the numerical simulation results.

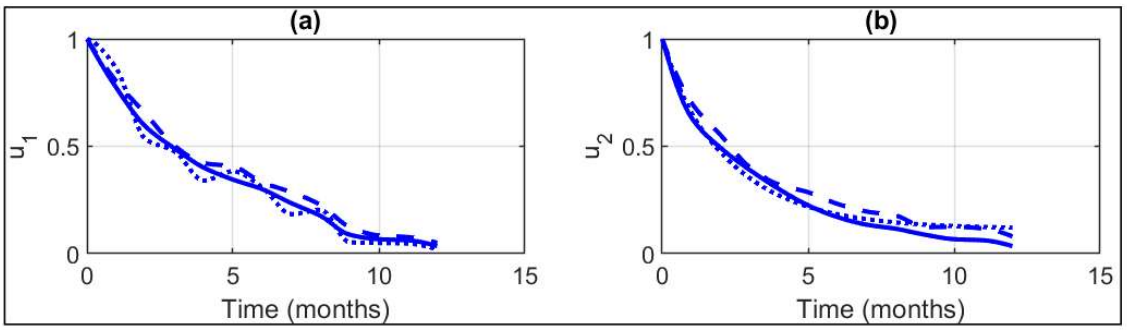

Figure 1: Trends of chemotherapies u_1 (a) and u_2 (b). Dotted line, dashed line and solid line curves show the variation of chemotherapy for the direct method, the fuzzy logic techniques and perturbation iteration method respectively.

The impact of chemotherapy is shown in the Figure 1 which illustrates both u_1 (Figure 1(a)) and u_2 (Figure 1(b)). These figures justify the trends during 12 months of treatment consummation by the patient. Their effect on the HBV dynamics is to prevent the virus and infected cells from producing new viruses respectively. The response of the administrated chemotherapy to the dynamics cells in HBV infection provides the trends of uninfected hepatocytes (Figure 2(a)),

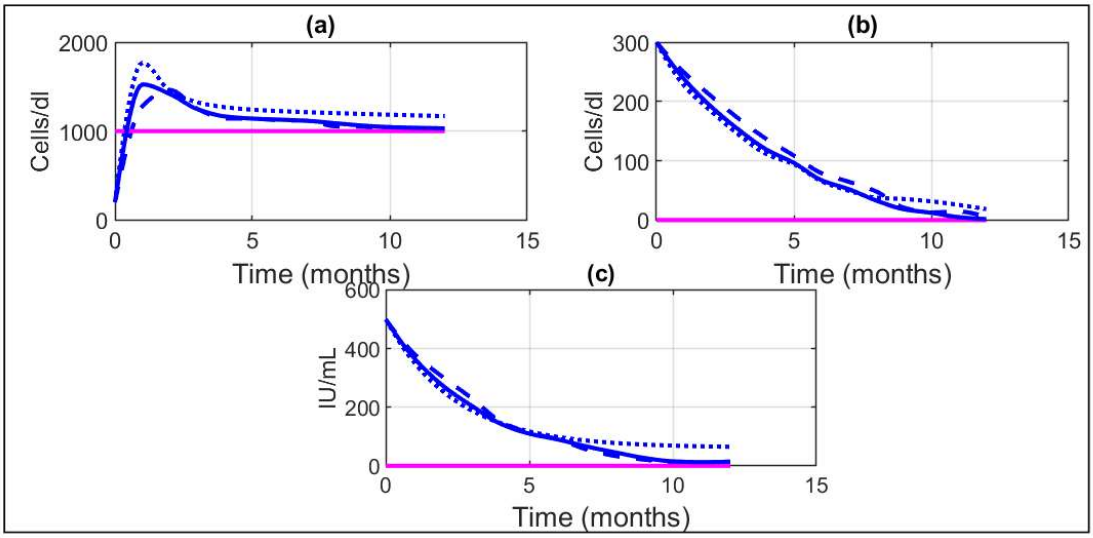

Figure 2: Trends of the concentration of uninfected hepatocytes (a), infected hepatocytes (b) and free virions (c). Dotted line, dashed line and solid line curves show the variation of chemotherapy for the direct method, the fuzzy logic techniques and perturbation iteration method respectively. The horizontal solid line illustrates the normal variation of concerned parameter.

infected hepatocytes (Figure 2(b)) and free virions (Figure 2(c)) respectively. The controls u_1 and u_2 are decreasing gradually from 1 (treatment is absent) and so that their variation is close to the value 0 (This value is the lowest and it means an appropriate use of therapy). During the first month of treatment uninfected hepatocytes increase to their higher value before decreasing to reach the normal number of cells of healthy subject (Figure 2(a)) due to action of therapeutic drugs. This response of therapy on HBV justifies the effectiveness of drugs to this liver infection that deals with this change in a chronically infected person's e-antigen status from positive to negative. The decrease of both infected hepatocytes and free virions after onset of therapeutic drugs to normal value is shown in Figures 2(b) and 2(c). The important role of treatment on HBV including hepatocellular carcinoma (HCC) is to boost the quality of specific immune responses and magnitude to improve the health of HBV patients to eliminate this liver infection and maintain immune homeostasis in patients. The basis for comparison of the three methods illustrated in Figures 1 and 2 shows that the results of the perturbation iteration method are close to two other used methods: the direct method and the fuzzy logic techniques. Consequently, the perturbation iteration method is an important tool to solve optimal controls problems. The findings of this work are rather satisfactory. Particularly, the response of the HBV infection to treatment can be formulated using an optimal control problem. Since the health of the patient under treatment shows reduced risk, therapeutic drugs play a crucial role so that any patient improves his/her health conditions.

5 Conclusion

In this work, three comparisons of numerical approaches have been made to find the optimal trajectories of uninfected hepatocytes, infected hepatocytes and free virions. These trajectories are the response of HBV treatment to the trends of hepatitis B dynamics. Particularly, the focus is made on the perturbation iteration method, which gives the optimal trajectories of HBV parameters in the same way as the two other methods. These methods provide satisfactory results, which are closed. Therefore, an optimal control problem can be solved using these methods. In particular, the response to treatment ensures the health of patients by providing optimal trajectories.

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Conflicts of Interest The authors declare that there is no conflict of interest for this paper.

References

[1] A. F. Adebisi, T. A. Ojurongbe, K. A. Okunlola & O. J. Peter (2021). Application of Chebyshev polynomial basis function on the solution of Volterra integro-differential equations using Galerkin method. *Mathematics and Computational Sciences*, *2*(4), 41–51. https://doi.org/10.30511/mcs.2021.540133.1047.

[2] W. M. Ahmad & R. El-Khazali (2007). Fractional-order dynamical models of love. *Chaos, Solitons & Fractals*, *33*(4), 1367–1375. https://doi.org/10.1016/j.chaos.2006.01.098.

[3] Y. Aksoy & M. Pakdemirli (2010). New perturbation–iteration solutions for Bratu-type equations. *Computers & Mathematics with Applications*, *59*(8), 2802–2808. https://doi.org/10.1016/j.camwa.2010.01.050.

[4] R. M. Anderson & R. M. May (1991). *Infectious diseases of humans: dynamics and control*. Oxford University Press, Oxford, UK.

[5] R. P. Beasley (1988). Hepatitis B virus. The major etiology of hepatocellular carcinoma. *Cancer*, *61*(10), 1942–1956. https://doi.org/10.1002/1097-0142(19880515)61:10<1942::AID-CNCR2820611003>3.0.CO;2-J.

[6] S. Bhattacharyya & S. Ghosh (2010). Optimal control of vertically transmitted disease: An integrated approach. *Computational and Mathematical Methods in Medicine*, *11*(4), Article ID 520830. https://doi.org/10.1155/2010/520830.

[7] K. Diethelm (2013). A fractional calculus based model for the simulation of an outbreak of dengue fever. *Nonlinear Dynamics*, *71*, 613–619. https://doi.org/10.1007/s11071-012-0475-2.

[8] A. Din (2021). The stochastic bifurcation analysis and stochastic delayed optimal control for epidemic model with general incidence function. *Chaos: An Interdisciplinary Journal of Nonlinear Science*, *31*(12), Article ID 123101. https://doi.org/10.1063/5.0063050.

[9] A. Din & Y. Li (2021). Lévy noise impact on a stochastic hepatitis B epidemic model under real statistical data and its fractal–fractional Atangana–Baleanu order model. *Physica Scripta*, *96*(12), Article ID 124008. https://doi.org/10.1088/1402-4896/ac1c1a.

[10] A. Din, Y. Li, F. M. Khan, Z. U. Khan & P. Liu (2022). On analysis of fractional order mathematical model of hepatitis B using Atangana–Baleanu Caputo (ABC) derivative. *Fractals*, *30*(01), Article ID 2240017. https://doi.org/10.1142/S0218348X22400175.

[11] A. Din, Y. Li, T. Khan & G. Zaman (2020). Mathematical analysis of spread and control of the novel corona virus (COVID-19) in China. *Chaos, Solitons & Fractals*, *141*, Article ID 110286. https://doi.org/10.1016/j.chaos.2020.110286.

[12] A. Din, Y. Li & A. Yusuf (2021). Delayed hepatitis B epidemic model with stochastic analysis. *Chaos, Solitons & Fractals*, *146*, Article ID 110839. https://doi.org/10.1016/j.chaos.2021.110839.

[13] A. Din, Y. Li, A. Yusuf & A. I. Ali (2022). Caputo type fractional operator applied to hepatitis B system. *Fractals*, *30*(01), 2240023. https://doi.org/10.1142/S0218348X22400230.

[14] A. Din, Y. Li, A. Yusuf, J. Liu & A. A. Aly (2022). Impact of information intervention on stochastic hepatitis B model and its variable-order fractional network. *The European Physical Journal Special Topics*, *231*(10), 1859–1873. https://doi.org/10.1140/epjs/s11734-022-00453-5.

[15] H. B. El-Serag (2012). Epidemiology of viral hepatitis and hepatocellular carcinoma. *Gastroenterology*, *142*(6), 1264–1273. https://doi.org/10.1053/j.gastro.2011.12.061.

[16] A. M. Elaiw, M. A. Alghamdi & S. Aly (2013). Hepatitis B virus dynamics: modeling, analysis, and optimal treatment scheduling. *Discrete Dynamics in Nature and Society*, *2013*, Article ID 712829. https://doi.org/10.1155/2013/712829.

[17] M. F. Faraloya, S. Shafie, F. M. Siam, R. Mahmud & S. O. Ajadi (2021). Numerical simulation and optimization of radiotherapy cancer treatments using the Caputo fractional derivative. *Malaysian Journal of Mathematical Sciences*, *15*(2), 161–187.

[18] M. Gahamanyi, W. Banzi & J. M. Ntaganda (2021). Solving an optimal control problem of hepatitis B virus dynamics: Efficacy of fuzzy logic strategy. *Rwanda Journal of Engineering, Science, Technology and Environment*, *4*(1), 1–18. https://doi.org/10.4314/rjeste.v4i1.1.

[19] M. M. Hassan, D. Li, A. S. El-Deeb, R. A. Wolff, M. L. Bondy, M. Davila & J. L. Abbruzzese (2008). Association between hepatitis B virus and pancreatic cancer. *Journal of Clinical Oncology*, *26*(28), 4557. https://doi.org/10.1200/JCO.2008.17.3526.

[20] K. Hattaf, M. Rachik, S. Saadi & N. Yousfi (2009). Optimal control of treatment in a basic virus infection model. *Applied Mathematical Sciences*, *3*(17-20), 949–958.

[21] C. Y. Ishola, O. A. Taiwo, A. F. Adebisi & O. J. Peter (2022). Numerical solution of two-dimensional Fredholm integro-differential equations by Chebyshev integral operational matrix method. *Journal of Applied Mathematics and Computational Mechanics*, *21*(1), 29–40. https://doi.org/10.17512/jamcm.2022.1.03.

[22] T. K. Kar & A. Batabyal (2011). Stability analysis and optimal control of an SIR epidemic model with vaccination. *Biosystems*, *104*(2–3), 127–135. https://doi.org/10.1016/j.biosystems.2011.02.001.

[23] T. K. Kar & S. Jana (2013). A theoretical study on mathematical modelling of an infectious disease with application of optimal control. *Biosystems*, *111*(1), 37–50. https://doi.org/10.1016/j.biosystems.2012.10.003.

[24] C. L. Lai & M. F. Yuen (2007). The natural history and treatment of chronic hepatitis B: A critical evaluation of standard treatment criteria and end points. *Annals of Internal Medicine*, *147*(1), 58–61. https://doi.org/10.7326/0003-4819-147-1-200707030-00010.

[25] J. Mann & M. Roberts (2011). Modelling the epidemiology of hepatitis B in New Zealand. *Journal of Theoretical Biology*, *269*(1), 266–272. https://doi.org/10.1016/j.jtbi.2010.10.028.

[26] G. F. Medley, N. A. Lindop, W. J. Edmunds & D. J. Nokes (2001). Hepatitis-B virus endemicity: Heterogeneity, catastrophic dynamics and control. *Nature Medicine*, *7*(5), 619–624. https://doi.org/10.1038/87953.

[27] M. Mirzazadeh (2016). A novel approach for solving fractional Fisher equation using differential transform method. *Pramana*, *86*, 957–963. https://doi.org/10.1007/s12043-015-1117-2.

[28] W. H. Organization et al. (2017). *Global hepatitis report 2017*. World Health Organization, Geneva.

[29] M. Pakdemirli, Y. Aksoy & H. Boyacı (2011). A new perturbation-iteration approach for first order differential equations. *Mathematical and Computational Applications*, *16*(4), 890–899. https://doi.org/10.3390/mca16040890.

[30] J. Pang, J. Cui & X. Zhou (2010). Dynamical behavior of a hepatitis B virus transmission model with vaccination. *Journal of Theoretical Biology*, *265*(4), 572–578. https://doi.org/10.1016/j.jtbi.2010.05.038.

[31] M. M. Salih & F. Ismail (2022). Trigonometrically-fitted fifth order four-step predictor-corrector method for solving linear ordinary differential equations with oscillatory solutions. *Malaysian Journal of Mathematical Sciences*, *16*(4), 739–748. https://doi.org/10.47836/mjms.16.4.07.

[32] B. S. Sheena, L. Hiebert, H. Han, H. Ippolito, M. Abbasi-Kangevari, Z. Abbasi-Kangevari, H. Abbastabar, A. Abdoli, H. A. Ali, M. M. Adane et al. (2022). Global, regional, and national burden of hepatitis B, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. *The Lancet Gastroenterology & Hepatology*, *7*(9), 796–829. https://doi.org/10.1016/S2468-1253(22)00124-8.

[33] M. Sheikhan & S. A. Ghoreishi (2013). Application of covariance matrix adaptation–evolution strategy to optimal control of hepatitis B infection. *Neural Computing and Applications*, *23*, 881–894. https://doi.org/10.1007/s00521-012-1013-3.

[34] X. Song & A. U. Neumann (2007). Global stability and periodic solution of the viral dynamics. *Journal of Mathematical Analysis and Applications*, *329*(1), 281–297. https://doi.org/10.1016/j.jmaa.2006.06.064.

[35] J. D. Stanaway, A. D. Flaxman, M. Naghavi, C. Fitzmaurice, T. Vos, I. Abubakar, L. J. Abu-Raddad, R. Assadi, N. Bhala, B. Cowie et al. (2016). The global burden of viral hepatitis from 1990 to 2013: Findings from the Global Burden of Disease Study 2013. *The Lancet*, *388*(10049), 1081–1088. https://doi.org/10.1016/S0140-6736(16)30579-7.

[36] S. Zhao, Z. Xu & Y. Lu (2000). A mathematical model of hepatitis B virus transmission and its application for vaccination strategy in China. *International Journal of Epidemiology*, *29*(4), 744–752. https://doi.org/10.1093/ije/29.4.744.