International Journal of Sciences

Research Article Volume 5 – June 2016 (06)

A Neural Network Approach for Solving Fractional-Order Model of HIV Infection of CD4+T-Cells

Samaneh Soradi Zeid[1], Mostafa Yousefi[2]

[1]Department of Mathematics, Faculty of Mathematics, University of Sistan and Baluchestan, Zahedan, Iran. e-mail:
[2]National Iranian Oil Products Distribution Company (NIOPDC), Zahedan Region, Zahedan, Iran.

Abstract—In this paper the perceptron neural networks are applied to approximate the solution of Fractional-order model of HIV infection of CD4+T-cells that includes a system of fractional differential equations (FDEs). We converted this model to a system of Volterra integral equations. Then, by using perceptron neural networks ability in approximating a nonlinear function, we propose approximating functions to approach parameters of this system of Volterra integral equations. By obtaining the approximated solution of this system, the unknown parameters of the original fractional HIV model are adjusted. Numerical results illustrate this approach is simple and accurate when applied to systems of FDEs.

Keywords: Fractional HIV infection model, Volterra integral equation, Perceptron neural networks, Fractional differential equation.

I. Introduction

Recently, fractional calculus (FC) has been extensively applied in many fields. Many mathematicians and applied researchers have tried to model real processes using the fractional calculus. Nigmatullin and Nelson described in terms of fractional kinetics in complex systems [10]. Jesus, Machado and Cunha analyzed the fractionalorder dynamics in botanical electrical impedances [5], [6]. Petrovic, Spasic and Atanackovic developed a fractional-order mathematical model of a human root dentin [8]. In biology, it has been deduced that the membranes of cells of biological organism have fractionalorder electrical conductance [7] and then are classified in groups of non-integer order models. Fractional derivatives embody essential features of cell rheological behavior and have enjoyed greatest success in the field of rheology [12]. The reason of using fractional order differential equationsisthattheyarenaturally related to systems with memory which exists in most biological systems and they are closely related to fractals which are abundant in biological systems. Also, it has been shown that modelling the behavior of brainstem vestibuleoculumotor neurons by FDEs has more advantages than classical integer-order modelling [11]. FDE are naturally related to systems with memory which exists in most biological systems. Also, they are closely related to fractals, which are abundant in biological systems [3].

The aim of this paper is to use the ability of perceptron neural networks in function approximation, to approximate the solution of fractional order model of HIV infection of CD4+T cells. The main motivation of using neural networks is that the use of neural networks provides differentiable solutions. In the next section we introduce some necessary preliminaries from model derivation. Section 3 introduces the neural network methodology as the approximation method. Numerical simulations are presented in section 4. Finally, conclusions are included in the last section.

II. Model derivation

Here, we introduce fractional-order into the model of HIV infection of CD4+T-cells [9]. This model is described by the following set of FDEs:

Published at: http://www.ijsciences.com/pub/issue/2016-06/
DOI: 10.18483/ijSci.1044; Online ISSN: 2305-3925; Print ISSN: 2410-4477

Samaneh Soradi Zeid (Correspondence)
s_soradi@yahoo.com
+

$$\begin{cases} D^{\alpha}T(t) = s - \mu_T T(t) + rT(t)\left(1 - \frac{T(t)+I(t)}{T_{max}}\right) - k_V T(t) \\ D^{\alpha}I(t) = k_1' V(t)T(t) - \mu_I I(t), \\ D^{\alpha}V(t) = N\mu_b I(t) - k_1 V(t)T(t) - \mu_V V(t), \end{cases} \quad (1)$$

with the initial conditions:

$$T(0) = T_0,\ I(0) = I_0,\ V(0) = V_0, (2)$$

where,

$$T_0 = \frac{r-\mu_T+[(r-\mu_T)^2+4rsT_{max}^{-1}]^{-1/2}}{2rT_{max}^{-1}}. (3)$$

In this model, T , I and V denote the concentration of uninfected CD4+T cells, infected CD4+T cells, and free HIV virus particles in the blood, respectively. We note that s is the source of CD4+T-cells from precursors, μ_T is the natural death rate of CD4+T-cells ($\mu_T T_{max} > s$, [2]), r is their growth rate (thus, $r > \mu_T$ in general), and T_{max} is their carrying capacity. The parameter k_1 represents the rate of infection of T-cells with free virus. k_1' is the rate at which infected cells become actively infected. μ_I is a blanket death term for infected cells, to reflect the assumption that we do not initially know whether the cells die naturally or by bursting. In addition, μ_b is the lytic death rate for infected cells. Since N viral particles are released by each lysing cell, this term is multiplied by the parameter N to represent the source for free virus (assuming a one-time initial infection). Finally, μ_V is the loss rate of virus. The parameters value of this FDE system is reported in Table 1.

TABLE 1: Variable and parameters for HIV infection model of CD4+t-cells.

Parameters	Description	Value/unit
μ_T	$Natural\ death\ rate\ of\ CD4+T$	$0.02\ day^{-1}$
μ_I	$Blanket\ death\ rate\ of\ infected\ CD4+T$	$0.26\ day^{-1}$
μ_V	Death rate of free virus	$2.4\ day^{-1}$
μ_b	Lytic death rate for infected cells	$0.24\ day^{-1}$
k_1	Rate CD4 + T become infected with virus	$2.4.10^{-5}mm^{-3}day^{-1}$
k_1'	$Rate\ infected\ cells\ become\ active$	$2\times10^{-5}mm^{-3}day^{-1}$
r	Growth rate of CD4 + T population	$0.03\ day^{-1}$
N	Number of virions produced by infected CD4 + T	$Varies$
T_{max}	Maximal population level of CD4 + T	$1500mm^{-3}$
s	Source term for uninfected CD4 + T	$10mm^{-3}day^{-1}$
T_0	CD4 + T population for HIV − negative persons	$1000mm^{-3}$

Throughout this paper, we set $D^{\alpha}(0 < \alpha \leq 1)$ as the Caputo fractional derivative of order α. Notice that, there are several approaches to the generalization of the notion of differentiation to fractional orders e.g. Riemann-Liouville, Caputo and Generalized Functions approach. For the concept of fractional derivative, we will adopt Caputos definition, which is a modification of the Riemann-Liouville definition and has the advantage of dealing properly with initial value problems. We first give the definition of fractional-order integration and fractional-order differentiation [4]: The fractional integral of order α of function $f \in C[a,b]$ is given by:

$$I^{\alpha}f(x) = \frac{1}{\Gamma(\alpha)}\int_0^x (x-\tau)^{\alpha-1}f(\tau)d\tau, (4)$$

where $I^0 f(x) = f(x), \alpha > 0,\ x > 0.$

Caputo fractional derivatives of order α, $n-1 < \alpha \leq n$, of function $f \in C[a,b]$ is given by:

$$D^0 f(x) = J^{m-\alpha}\left(\frac{d^m}{dx^m}f(x)\right), (5)$$

where $m \in N$ and $m-1 \leq \alpha \leq m$. The following theorem, helps us to apply a fractional integral over a fractional derivative. [1]. Let $\alpha > 0$ and $= [\alpha]$. If $f(x) \in C^n[a,b]$; then:

$$I^{\alpha}(D^{\alpha}f)(x) = f(x) - \sum_{k=0}^{n-1}\frac{f^{(k)}(a)}{k!}(x-a)^k. (6)$$

In particular, if $0 < \alpha \leq 1$ and $f(x) \in C[a,b]$, then:

$$I^{\alpha}(D^{\alpha}f)(x) = f(x) - f(a). (7)$$

By applying fractional integral operator for the first equation of (1), we have:

$$I^{\alpha}(D^{\alpha}T) = I^{\alpha}\left(s - \mu_T T(t) + rT(t)\left(1 - \frac{T(t)+I(t)}{T_{max}}\right) - k_V T(t)\right). (8)$$

According to Theorem II and definition of fractional integral we have:

$$T(t) - T(0) = \frac{1}{\Gamma(\alpha)}\int_a^t (t-\tau)^{\alpha-1}\left(s - \mu_T T(\tau) + rT(\tau)\left(1 - \frac{T(\tau)+I(\tau)}{T_{max}}\right) - k_V T(\tau)\right)d\tau, (9)$$

or equivalently it can be rewritten as the following Volterra integral equation:

$$T(t) = T(0) + \frac{1}{\Gamma(\alpha)}\int_a^t (t-\tau)^{\alpha-1}\left(s - \mu_T T(\tau) + rT(\tau)\left(1 - \frac{T(\tau)+I(\tau)}{T_{max}}\right) - k_V T(\tau)\right)d\tau. \quad (10)$$

Following a similar approach, the second and third equation of (1) with initial conditions (2), can be converted to the following Volterra integral equations, respectively:

$$I(t) = \frac{1}{\Gamma(\alpha)}\int_a^t (t-\tau)^{\alpha-1}\left(k_1' V(\tau)T(\tau) - \mu_I I(\tau)\right)d\tau, \quad (11)$$

$$V(t) = \frac{1}{\Gamma(\alpha)}\int_a^t (t-\tau)^{\alpha-1}\left(N\mu_b I(\tau) - k_1 V(\tau)T(\tau) - \mu_V V(\tau)\right)d\tau. \quad (12)$$

III. Approximation Method

To solve the farctional HIV infection of CD4+T-cells (1)-(2), by using the mathematical structure of a single layer neural networks, we can consider the following approximate functions for the concentration of uninfected CD4+T cells, infected CD4+T cells, and free HIV virus particles in the blood, respectively, by:

$$\begin{cases} T_N(t,\psi_T) = A(t) + B(t)N(t,\psi_T) \\ I_N(t,\psi_I) = C(t) + D(t)N(t,\psi_I) \\ V_N(t,\psi_V) = F(t) + G(t)N(t,\psi_V), \end{cases} \quad (13)$$

where $A(t)$, $B(t)$, $C(t)$, $D(t)$, $F(t)$ and $(G(t)$ are real single variable functions such that the approximate functions T_N, I_N and V_N satisfy the initial condition (2). For example, if $T(0) = 0$ then we must choose $A(t)$ and $B(t)$ such that $T\_N(0,\psi_N) = 0$, thus we can choose $A(t) = 0$ and $B(t) = t$. Also, ψ_T, ψ_I and ψ_V are the corresponding weight vectors containing the weighta of $T(t)$, $I(t)$ and $V(t)$, respectively. By substituting the above approximate functions in (10)-(12) we get:

$$\begin{cases} T_N(t,\psi_T) = T_0 + \frac{1}{\Gamma(\alpha)}\int_a^t (t-\tau)^{\alpha-1}(s - \mu_T T_N(\tau,\psi_T) \\ \qquad + rT_N(\tau,\psi_T)\left(1 - \frac{T_N(\tau,\psi_T)+I_N(\tau,\psi_T)}{T_{max}}\right) - k_V T_N(\tau,\psi_T))d\tau \\ I_N(t,\psi_I) = \frac{1}{\Gamma(\alpha)}\int_a^t (t-\tau)^{\alpha-1}\left(k_1' V_N(\tau,\psi_V)T_N(\tau,\psi_T) - \mu_I I_N(\tau,\psi_I)\right)d \\ V_N(t,\psi_V) = \frac{1}{\Gamma(\alpha)}\int_a^t (t-\tau)^{\alpha-1}\left(N\mu_b I_N(\tau,\psi_I) - k_1 V_N(\tau,\psi_V)T_N(t,\psi_T) - \mu_V V_N(\tau,\psi_V)\right)d\tau. \end{cases} \quad (14)$$

Now, we look for an approximation for functions T_N, I_N and V_N. To solve (14) we introduce the following squared residual error functions:

$$\begin{cases} R_T(t,\psi) = [T_N(t,\psi_T) - T_0 - \frac{1}{\Gamma(\alpha)}\int_a^t (t-\tau)^{\alpha-1}(s - \mu_T T_N(\tau,\psi_T) \\ \qquad + rT_N(\tau,\psi_T)\left(1 - \frac{T_N(\tau,\psi_T)+I_N(\tau,\psi_T)}{T_{max}}\right) - k_V T_N(\tau,\psi_T))d\tau]^2 \\ R_I(t,\psi) = [I_N(t,\psi_I) - \frac{1}{\Gamma(\alpha)}\int_a^t (t-\tau)^{\alpha-1}\left(k_1' V_N(\tau,\psi_V)T_N(\tau,\psi_T) - \mu_I I_N(\tau,\psi_I)\right)d\tau]^2 \\ R_V(t,\psi) = [V_N(t,\psi_V) - \frac{1}{\Gamma(\alpha)}\int_a^t (t-\tau)^{\alpha-1}\left(N\mu_b I_N(\tau,\psi_I) - k_1 V_N(\tau,\psi_V)T_N(t,\psi_T) - \mu_V V_N(\tau,\psi_V)\right)d\tau]^2, \end{cases} \quad (15)$$

where $\psi = (\psi_T, \psi_I, \psi_V)$ is a vector containing all weights of three approximator functions (13). To solve (15), we divide the interval $[a, b]$ into m subinterval and calculate the integrals in any subintervals, by using any numerical integration technique such as Simpson's rule. Then, we introduce the following unconstrained optimization problem:

$$\min_{\psi} R(\psi) = \sum_{i=1}^{m}[R_T(t_i,\psi) + R_I(t_i,\psi) + R_V(t_i,\psi)], \quad (16)$$

which can be solved by any classical mathematical optimization algorithm such as Quasi-Newton methods that we use in this paper. Suppose that $\psi^* = (\psi_T^*, \psi_I^*, \psi_V^*)$ is the optimal solution of optimization problem (16). Since the neural networks are universal approximators, the obtained weights are convergent to the optimal values. This concept is illustrated in numerical examples by plotting the convergence of the weights. Substituting these optimal weights into the corresponding approximate functions T_N, I_N and V_N in (13), we get the following final approximated solution of fractional HIV infection of CD4+T-cells (1)-(2):

$$\begin{cases} T_N(t,\psi_T^*) = A(t) + B(t)N(t,\psi_T^*) \\ I_N(t,\psi_I^*) = C(t) + D(t)N(t,\psi_I^*) \\ V_N(t,\psi_V^*) = F(t) + G(t)N(t,\psi_V^*). \end{cases} \quad (17)$$

We mention that to attain more accurate solutions, we can use more neurons or use any heuristic optimization algorithm.

IV. Numerical Results

In this section, by using the ability of perceptron neural network model in approximating the solution of fractional model of HIV infection of CD4+T-cells (1) while considering the conditions (2), we propose the following approximation functions:

$$\begin{cases} T_N(t,\psi_T) = T_0 + tN(t,\psi_T) \\ I_N(t,\psi_I) = tN(t,\psi_I) \\ V_N(t,\psi_V) = tN(t,\psi_V). \end{cases} \quad (18)$$

It is easy to check that the proposed approximate functions TN, IN and VN satisfy the boundary conditions $T_N(0,\psi_T) = T_0, I_N(0,\psi_I) = 0$ and $V_N(0,\psi_V) = 0$. Now, we rewrite (15) for this approximation functions and finally solve the optimization problem (16) for $m = 350$. To show the convergence of the weights vector ψ during the optimization step, the values of ψ are plotted in Fig. 1.

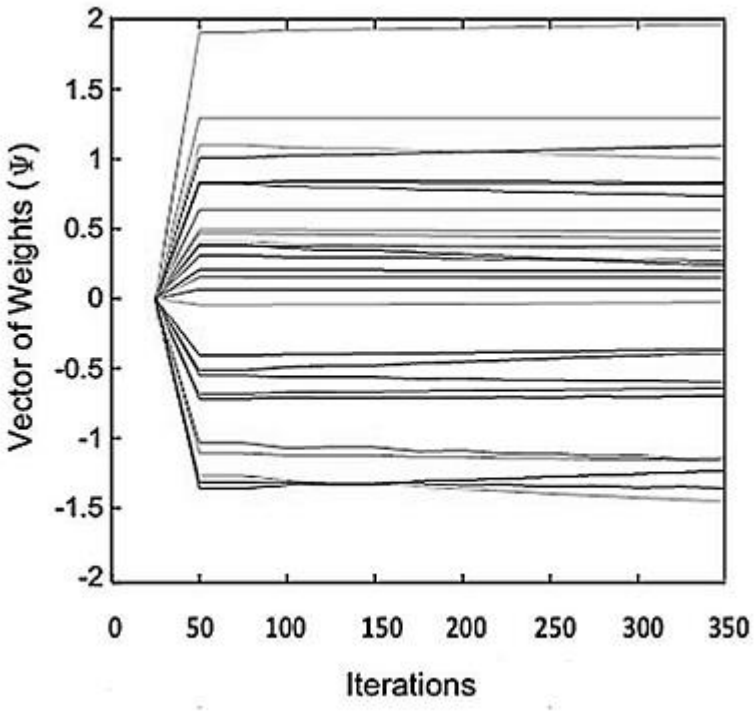

Fig. 1. Covergence of the weights vector ψ during the optimization step.

Also, Fig. 2 illustrate the approximate values of T , I and V for several values of derivative order α and it is shown that when $\alpha \to 1$ the solution of the fractional model (1)-(2), reduce to the standard solution $T(t)$, $I(t)$ and $V(t)$.

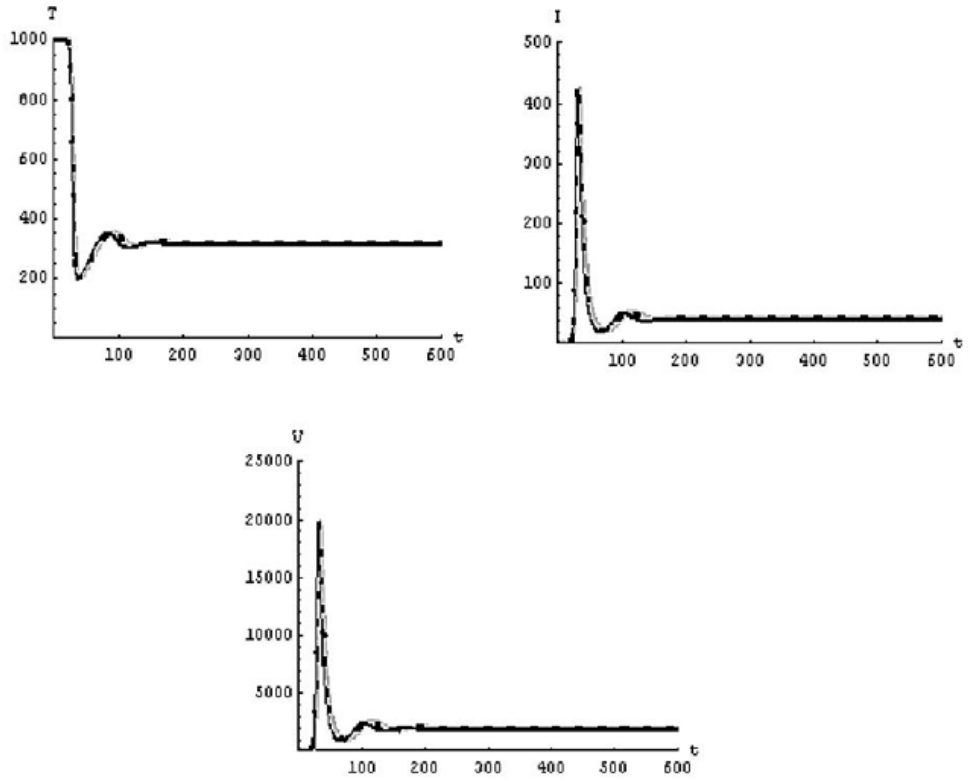

Fig. 2. The concentration of the uninfected (T) and infected CD4+T cells(I) and free HIV virus particles (V) with various choices of α: Gray solid line ($\alpha = 1$), Dotted line ($\alpha = .99$), Black solid line ($\alpha = .95$).

V. Conclusions

In this paper, we employed the neural networks approach for studying the approximate solutions of nonlinear ordinary differential equations system of fractional order such as human T-cell lymphotropic virus HIV infection of CD4+T-cells. We demonstrated the accuracy and efficiency of these methods by solving some ordinary differential equation systems of fractional order. From the obtained results in the presented figures, it is clear that in the primary stage of the infection with the HIV virus, a dramatically decrease in the level of the CD4+T-cells occurs because of the death of such infected cells. On the other hand, the number of the free HIV virus particles and the number of susceptible CD4+T-cells increase. This assumes that the growth of healthy T-cells slows down during the course of HIV infection.

REFERENCES

1) A. A. Kilbas, H. M. Srivastava and J. J. Trujillo, Theory and applications of fractional differential equations, (Vol. 204). (2006) Elsevier Science Limited.
2) A.S. Perelson, D.E. Kirschner, R. De Boer, Dynamics of HIV infection of CD4+T-cells, Mathematical Bioscience 114 (1993) 81-125.
3) E. Ahmed, A.S. Elgazzar, On fractional order differential equations model for nonlocal epidemics, Physica A 379 (2007) 607-614.
4) I. Podlubny, Fractional Differential Equations, Academic Press, New York, 1999.
5) I.S. Jesus, J.A.T. Machado, J.B. Cunha, Fractional electrical impedances in botanical elements, Journal of Vibration and Control 14 (2008) 1389-1402.
6) I.S. Jesus, J.A.T. Machado, J.B. Cunha, Fractional order electrical impedance of fruits and vegetables, in: Proceedings of the 25th IASTED International Conference MODELLING, IDENTIFICATION, AND CONTROL, February 6-8, 2006, Lanzarote, Canary Islands, Spain.
7) K.S. Cole, Electric conductance of biological systems, in: Proc. Cold Spring Harbor Symp. Quant. Biol, Cold Spring Harbor, New York, 1993, pp. 107-116.
8) L.M. Petrovic, D.T. Spasic, T.M. Atanackovic, On a mathematical model of a human root dentin, Dental Materials 21 (2005) 125-128 .
9) R.V. Culshaw, S. Ruan, A delay-differential equation model of HIV infection of CD4+T-cells, Mathematical Bioscience 165 (2000) 27-39.
10) R.R. Nigmatullin, S.O. Nelson, Recognition of the fractional kinetics in complex systems: Dielectric properties of fresh fruits and vegetables form 0.01 to1.8 GHz, Signal Processing 86 (2006) 2744-2759.
11) T.J. Anastasio, The fractional-order dynamics of bainstem vestibulooculomotor neurons, Biological Cybernetics 72 (1994) 69-79.
12) V.D. Djordjevi, J. Jari, B. Fabry, J.J. Fredberg, D. Stamenovi, Fractional derivatives embody essential features of cell rheological behavior, Annals of Biomedical Engineering 31 (2003) 692-699.