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\textbf{Abstract}—In this paper the perceptron neural networks are applied to approximate the solution of Fractional-order model of HIV infection of CD4\textsuperscript{+}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.

\textbf{Keywords}: Fractional HIV infection model, Volterra integral equation, Perceptron neural networks, Fractional differential equation.

\section{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 \cite{10}. Jesus, Machado and Cunha analyzed the fractional-order dynamics in botanical electrical impedances \cite{5}, \cite{6}. Petrovic, Spasic and Atanackovic developed a fractional-order mathematical model of a human root dentin \cite{8}. In biology, it has been deduced that the membranes of cells of biological organism have fractional-order electrical conductance \cite{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 \cite{12}. The reason of using fractional order differential equations is that they are naturally related to systems with memory which exists in most biological systems and they are closely related to fractals which are abundant in biological systems \cite{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\textsuperscript{+}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.

\section{II. Model derivation}

Here, we introduce fractional-order into the model of HIV infection of CD4\textsuperscript{+}T-cells \cite{9}. This model is described by the following set of FDEs:
The model is given by

\[
\begin{align*}
D^\alpha T(t) &= s - \mu_T T(t) + r T(t) \left(1 - \frac{T(t) + I(t)}{T_{\text{max}}}ight) - k_Y T(t) \\
D^\alpha I(t) &= k_1 V(t) T(t) - \mu_I I(t), \\
D^\alpha V(t) &= N \mu_b I(t) - k_Y V(t) T(t) - \mu_V V(t),
\end{align*}
\]

with the initial conditions:

\[ T(0) = T_0, \ I(0) = I_0, \ V(0) = V_0, \]

where,

\[ T_0 = \frac{r - \mu_T + (r - \mu_T)^2 + 4r T_{\text{max}}^2}{2r T_{\text{max}}^2}. \]

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, \( \mu_T \) is the natural death rate of CD4+T-cells (\( \mu_T T_{\text{max}} > s \), [2]), \( r \) is their growth rate (thus, \( r > \mu_T \) in general), and \( T_{\text{max}} \) 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. \( \mu_I \) 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, \( \mu_b \) 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, \( \mu_V \) 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.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Description</th>
<th>Value/unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \mu_T )</td>
<td>Natural death rate of CD4+T</td>
<td>0.02 day(^{-1})</td>
</tr>
<tr>
<td>( \mu_I )</td>
<td>Blanket death rate of infected CD4+T</td>
<td>0.26 day(^{-1})</td>
</tr>
<tr>
<td>( \mu_V )</td>
<td>Death rate of free virus</td>
<td>2.4 day(^{-1})</td>
</tr>
<tr>
<td>( \mu_b )</td>
<td>Lytic death rate for infected cells</td>
<td>0.24 day(^{-1})</td>
</tr>
<tr>
<td>( k_1 )</td>
<td>Rate CD4+T become infected with virus</td>
<td>2.4 \times 10^{-5} \text{mm}^{-3} \text{day}^{-1})</td>
</tr>
<tr>
<td>( k'_1 )</td>
<td>Rate infected cells become active</td>
<td>2 \times 10^{-5} \text{mm}^{-3} \text{day}^{-1})</td>
</tr>
<tr>
<td>( r )</td>
<td>Growth rate of CD4+T population</td>
<td>0.03 day(^{-1})</td>
</tr>
<tr>
<td>( N )</td>
<td>Number of virions produced by infected CD4+T</td>
<td>\text{Varies}</td>
</tr>
<tr>
<td>( T_{\text{max}} )</td>
<td>Maximal population level of CD4+T</td>
<td>1500mm(^{-3})</td>
</tr>
<tr>
<td>( s )</td>
<td>Source term for uninfected CD4+T</td>
<td>0 \text{mm}^{-3} \text{day}^{-1})</td>
</tr>
<tr>
<td>( T_0 )</td>
<td>CD4+T population for HIV−negative persons</td>
<td>1000mm(^{-3})</td>
</tr>
</tbody>
</table>

Throughout this paper, we set \( D^\alpha (0 < \alpha \leq 1) \) as the Caputo fractional derivative of order \( \alpha \). 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 \( \alpha \) of function \( f \in \mathcal{C}[a , b] \) is given by:

\[ I^\alpha f(x) = \frac{1}{\Gamma(\alpha)} \int_a^x (x - \tau)^{\alpha - 1} f(\tau) d\tau \],

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

Caputo fractional derivatives of order \( \alpha, n - 1 < \alpha \leq n \), of function \( f \in \mathcal{C}[a , b] \) is given by:

\[ D^\alpha f(x) = f^{(n)}(x) \left( \frac{\alpha}{\alpha - n} \right) \left( \frac{d}{dx} \right)^{n-\alpha} f(x) \],

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 \( = \lfloor \alpha \rfloor \). If \( f(x) \in \mathcal{C}^m[a , b] \); then:

\[ I^\alpha (D^\alpha f)(x) = f(x) - \sum_{k=0}^{m-1} \frac{f^{(k)}(a)}{k!} (x-a)^k \],

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

\[ I^\alpha (D_0^\alpha f)(x) = f(x) - f(a) \].

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

\[ I^\alpha (D^\alpha T) = I^\alpha \left( s - \mu_T T(t) + r T(t) \left(1 - \frac{T(t) + I(t)}{T_{\text{max}}}ight) - k_Y T(t) \right). \]

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

\[ T(t) - T(0) = \frac{1}{\Gamma(\alpha)} \int_0^t (t - \tau)^{\alpha - 1} \left( s - \mu_T T(t) + r T(t) \left(1 - \frac{T(t) + I(t)}{T_{\text{max}}}ight) - k_Y T(t) \right) d\tau \],

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

http://www.ijSciences.com  Volume 5 – June 2016 (06)
A Neural Network Approach for Solving Fractional-Order Model HIV Infection of CD4+T-Cells

\[ T(t) = T(0) + \frac{1}{\Gamma(\alpha)} \int_0^t (t - \tau)^{\alpha - 1} \left( s - \mu_T T(\tau) + rT(\tau) \left( 1 - \frac{\tau(\tau+1)}{\tau_{max}} \right) - k_V T(\tau) \right) d\tau. \quad (10) \]

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:

\[ I(t) = \frac{1}{\Gamma(\alpha)} \int_0^t (t - \tau)^{\alpha - 1} \left( k_1 V(t) T(\tau) - \mu I(t) \right) d\tau, \quad (11) \]

\[ V(t) = \frac{1}{\Gamma(\alpha)} \int_0^t (t - \tau)^{\alpha - 1} \left( N \mu_p I(\tau) - k_i V(t) T(\tau) - \mu_V V(t) \right) d\tau. \quad (12) \]

III. Approximation Method

To solve the fractional 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:

\[
\begin{align*}
T_N(t, \psi_T) &= A(t) + B(t)N(t, \psi_T) \\
I_N(t, \psi_I) &= C(t) + D(t)N(t, \psi_I) \\
V_N(t, \psi_V) &= F(t) + G(t)N(t, \psi_V),
\end{align*}
\]

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, \( \psi_T, \psi_I \) and \( \psi_V \) are the corresponding approximate functions for the concentration of uninfected CD4+T cells, infected CD4+T cells, and free HIV virus particles in the blood, respectively. By substituting the above approximate functions in (10)-(12) we get:

\[
\begin{align*}
T_N(t, \psi_T) &= T_0 + \frac{1}{\Gamma(\alpha)} \int_0^t (t - \tau)^{\alpha - 1} \left( s - \mu_T T_N(\tau, \psi_T) \right) \\
&\quad + rT_N(\tau, \psi_T) \left( 1 - \frac{\tau_N(\tau, \psi_T) + I_N(\tau, \psi_I)}{\tau_{max}} \right) - k_V T_N(\tau, \psi_T) d\tau,
\end{align*}
\]

\[
\begin{align*}
I_N(t, \psi_I) &= \frac{1}{\Gamma(\alpha)} \int_0^t (t - \tau)^{\alpha - 1} \left( k_1 V_N(\tau, \psi_V) T_N(\tau, \psi_T) - \mu_I I_N(\tau, \psi_I) \right) d\tau, \\
V_N(t, \psi_V) &= \frac{1}{\Gamma(\alpha)} \int_0^t (t - \tau)^{\alpha - 1} \left( N \mu_p I_N(\tau, \psi_I) - k_i V_N(\tau, \psi_V) T_N(\tau, \psi_T) - \mu_V V_N(\tau, \psi_V) \right) d\tau.
\end{align*}
\]

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:
\[
\begin{align*}
T_N(t, \psi_T) &= T_0 + tN(t, \psi_T) \\
I_N(t, \psi_I) &= tN(t, \psi_I) \\
V_N(t, \psi_V) &= tN(t, \psi_V).
\end{align*}
\]

(18)

It is easy to check that the proposed approximate functions \(T_N, I_N\) and \(V_N\) 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 \(\psi\) during the optimization step, the values of \(\psi\) are plotted in Fig. 1.

![Fig. 1. Coverage of the weights vector \(\psi\) during the optimization step.](image)

Also, Fig. 2 illustrate the approximate values of \(T, I\) and \(V\) for several values of derivative order \(\alpha\) 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 \(V(t)\).
A Neural Network Approach for Solving Fractional-Order Model HIV Infection of CD4+T-Cells

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