

Numerical Treatments for a Complex Order Fractional HIV Infection Model with Drug Resistance During Therapy

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Abstract: In this article, we develop a numerical technique for solving HIV mathematical model of complex order with drug resistance during the therapy treatment, where the derivative is defined in Caputo sense. Two numerical methods are presented to numerically investigate the complex order fractional HIV model. The proposed numerical methods are the non-standard finite difference method and the generalized Euler method. Comparative studies and numerical simulations are presented to validate the theoretical results.

Keywords: Fractional complex order HIV infection model, nonstandard finite difference method, generalized Euler method, positive solutions, drug resistance.

1 Introduction, motivation and preliminaries

The complex order fractional derivative can be considered as a generalization of the integer order derivative and fractional order derivative [1] when the imaginary part of complex order equals to zero. A new model for HIV infection is investigated, in [2] where the derivatives are defined as complex order fractional derivatives.

The human immunodeficiency virus (HIV) is a retrovirus that declines the restraint of the immune system. The HIV power results virus in its wide replication during the acute stage. The next band of the HIV infection is the chronic stage. For more details on the model problem see [3], [4].

The five major medicine classes, that damage HIV/AIDS are the protease inhibitors (PI), the multi-drug inhibitors (MI), the fusion/entry inhibitors (FEI), and the reverse transcriptase inhibitors (RTI), integrate inhibitors (II).

The nonstandard finite difference method (NSFDM) is proposed by Mickens ([5]-[12]). In addition, the NSFDM is used to solve fractional order systems. For more details, see [13]- [16]).

The main contribution of this work is to develop an efficient numerical algorithm for approximating the solutions of the fractional complex order model which is given in [2]. Comparative studies between NSFDM and the generalized Euler method (GEM) are given. Simulations for the fractional complex order model are given.

The rest of this paper is structured as follows: In Section 2, fractional complex order definitions and NSFDM are given. In Section 3, the HIV fractional complex order model is presented. In Section 4, some properties of the solution of the proposed model are addressed. In Section 5, the NSFDM is constructed for the proposed model, the positivity and the boundedness are proved. The applicability and efficiency of NSFDM are given in Section 6. Finally, conclusion is presented in Section 7.

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2 Mathematical tools

In this section, we recall some important definitions of the complex calculus and the NSFDM which are used in the remaining section of this paper

2.1 Complex order calculus

Consider the following fractional complex order differential equation:

$${}_0^C D_t^z f(t) = y(t, f(t)), \quad f(0) = f_0, \quad z \in \mathbb{C}. \quad (1)$$

There are three definitions for the derivative of the complex order namely Grünwald–Letnikov’s definition (GL), the Riemann-Liouville and the Caputo definition. The Caputo derivative of complex order is given as follows [17] :

$${}_0^C D_t^z f(t) = \begin{cases} \frac{d^z f(t)}{dt^z}, & \text{if } z \in \mathbb{N}, \\ {}_0^C D_t^{z - [Re(z)]} {}_0^C D_t^{[Re(z)]} f(t), & \text{if } Re(z) \in \mathbb{R}^+ \text{ and } z \notin \mathbb{N}, \\ {}_0^C D_t^{z-1} \frac{df(t)}{dt}, & \text{if } Re(z) = 0 \text{ and } \Im(z) \neq 0, \\ f(t), & \text{if } z = 0, \\ \frac{1}{\Gamma(1-\alpha)} \int_0^t (t-s)^{-\alpha} f'(s) ds, & \text{if } Re(z), \Im(z) \in \mathbb{R}, \\ \int_c^t \frac{(t-s)^{-z-1}}{\Gamma(-z)} f(s) ds, & \text{if } Re(z) \in \mathbb{R}^-. \end{cases} \quad (2)$$

The Stirling asymptotic formula of gamma function for $z \in \mathbb{C}$ is given as follows [18]:

$$\Gamma(z) = (2\pi)^{\frac{1}{2}} z^{z-\frac{1}{2}} (e)^{-z} \left[1 + O\left(\frac{1}{z}\right) \right], \quad |\arg(z)| < \pi; |z| \rightarrow \infty. \quad (3)$$

The Grünwald–Letnikov’s complex order derivatives is given as follows [17] :

$${}_0^C D_t^{z-1} \frac{df(t)}{dt} = \lim_{h \rightarrow 0^+} \frac{\sum_{k=0}^{[\frac{t-c}{h}]} (-1)^k \binom{z}{k} f(t-kh)}{h^z}, \quad (4)$$

where

$$\binom{z}{k} = \begin{cases} \frac{\Gamma(z+1)}{\Gamma(k+1)\Gamma(z-k+1)}, & \text{if } z, k, z-k \in \mathbb{C} \setminus \mathbb{Z}^-, \\ \frac{(-1)^k \Gamma(k-z)}{\Gamma(k+1)\Gamma(z-k+1)}, & \text{if } z \in \mathbb{Z}^- \text{ and } k \in \mathbb{Z}_0^+, \\ 0, & \text{if } (k \in \mathbb{Z}^- \text{ or } k-z \in \mathbb{N}) \text{ and } z \notin \mathbb{Z}^-. \end{cases}$$

We extend the generalized Euler method (GEM) to complex fractional order $z \in \mathbb{C}$ when $t_{j+1} = t_j + h$ and using (3) as follows :

$$y(t_{j+1}) = y(t_j) + f(t_j, y(t_j)) \frac{h^z}{\Gamma(z+1)}. \quad (5)$$

2.2 NSFDM

The NSFDM can preserve the properties of the exact solution of the studies ordinary differential equations (ODEs) or partial differential equations (PDEs). We point out here that using Euler method to approximate $\frac{dy}{dt}$, we will replace $\frac{y(t+h)-y(t)}{h}$ by $\frac{y(t+h)-y(t)}{\phi(h)}$, where $\phi(h)$ is a continuous function,

$$\phi(h) = h + O(h^2). \quad (6)$$

Also, the nonlinear terms are replaced as in the following example:

$$yx \rightarrow \begin{cases} y_n x_{n+1}, \\ y_{n+1} x_n. \end{cases}$$

3 Complex order HIV model

The fractional complex order model is given as follow:

$$\begin{aligned}
 \frac{1}{2}({}_0^C D_t^{\alpha+i\beta} + {}_0^C D_t^{\alpha-i\beta})T(t) &= -(k_r(1 - n_{rr}^r)T(t)V_r(t) + k_s(1 - n_{rr}^s)T(t)V_s(t) - f(T)), \\
 \frac{1}{2}({}_0^C D_t^{\alpha+i\beta} + {}_0^C D_t^{\alpha-i\beta})T_s(t) &= ((1 - u)k_s(1 - n_{rr}^s - \delta T_s(t))T(t)V_s(t)), \\
 \frac{1}{2}({}_0^C D_t^{\alpha+i\beta} + {}_0^C D_t^{\alpha-i\beta})V_s(t) &= -(cV_s(t) - N_s\delta(1 - n_p^s)T_s(t)), \\
 \frac{1}{2}({}_0^C D_t^{\alpha+i\beta} + {}_0^C D_t^{\alpha-i\beta})V_r(t) &= (-\delta T_r(t) + k_r(1 - n_{rr}^r)T(t)T_r(t) + uk_s(1 - n_{rr}^s)V_s(t)T(t)), \\
 \frac{1}{2}({}_0^C D_t^{\alpha+i\beta} + {}_0^C D_t^{\alpha-i\beta})V_r(t) &= -(cV_r(t) - N_r\delta(1 - n_p^r)T_r),
 \end{aligned} \tag{7}$$

where, the uninfected target cells T is given as follows [19]:

$$f(T) = \begin{cases} f_1(t) = r(1 - \frac{T}{T_{max}}) - (dT - \lambda), \\ f_2(t) = r(1 - \frac{T+T_s+T_r}{T_{max}}) - (dT - \lambda), \\ f_3(t) = -(dT - \lambda). \end{cases} \tag{8}$$

The definitions of all variables and parameters are given in Tables 1 and 2 respectively. For more details for this model see [2]. The initial conditions are given as follows:

$$T_s(0) \geq 0, T(0) \geq 0, V_s(0) \geq 0, V_r(0) \geq 0, T_r(0) \geq 0,$$

Table 1: HIV model variables [2].

Variable	Definition
V_s	Infectious viruses of drug-sensitive
T_s	Infected $CD4^+T$ drug-sensitive cells
T_r	Infected $CD4^+T$ drug-resistant cells
T	Uninfected $CD4^+T$ populations cells
V_r	Infectious viruses of drug-resistant

Table 2: HIV model parameters [2]

Parameter	Value	Definition
λ	75	The production rate of T cells .
d	0.1	The death rate of T .
r	0.03	The rate of proliferate of T .
T_{max}	1500	T carrying capacity.
k_s	2.4×10^{-6}	The rate of infected by V_s .
k_r	2×10^{-6}	The rate of infected by V_r .
u	3×10^{-5}	The rate of proliferate of T (in absence of the infected T cells or virus) .
δ	1	Death of infected cell.
N_s	4800	Bursting sizes of drug-sensitive strain.
N_r	4000	Bursting sizes of drug-resistant strain.
c	23	The rate of the cleared the viruses.
n_{rt}^s	0.4	The rate efficacy of RTI for wild type.
n_{rt}^r	0.2	The rate efficacy of RTI for mutants.
n_p^r	0.1	The efficacy of PI for mutants.
n_p^s	0.1	PI efficacy of wildtype strain.

4 Properties of the solutions of the proposed model

4.1 Stability analysis

The disease-free equilibrium is defined as the point at which no disease is present in the population ($T_r = 0$), which is represented in the model as

$$\begin{aligned}
 \frac{1}{2}({}_0^C D_t^{\alpha+i\beta} + {}_0^C D_t^{\alpha-i\beta})T(t) &= 0, \\
 \frac{1}{2}({}_0^C D_t^{\alpha+i\beta} + {}_0^C D_t^{\alpha-i\beta})T_s(t) &= 0, \\
 \frac{1}{2}({}_0^C D_t^{\alpha+i\beta} + {}_0^C D_t^{\alpha-i\beta})V_s(t) &= 0, \\
 \frac{1}{2}({}_0^C D_t^{\alpha+i\beta} + {}_0^C D_t^{\alpha-i\beta})T_r(t) &= 0, \\
 \frac{1}{2}({}_0^C D_t^{\alpha+i\beta} + {}_0^C D_t^{\alpha-i\beta})V_r(t) &= 0.
 \end{aligned} \tag{9}$$

The disease free equilibrium point of system (7) is

$$\xi_1 = \left(\frac{\lambda + r}{d + \frac{r}{T_{max}}}, 0, 0, 0, 0 \right).$$

The Jacobian matrix J for this system evaluated at the equilibrium point is:

$$J = \begin{pmatrix} -d - \frac{r}{T_{max}} - k_s(1-n_{rt}^s)V_s - k_r(1-n_{rt}^r)V_r & 0 & -k_s(1-n_{rt}^s)T & 0 & -k_r(1-n_{rt}^r)T \\ (1-u)k_s(1-n_{rt}^s)V_s & -\delta & (1-u)k_s(1-n_{rt}^s)T & 0 & 0 \\ 0 & N_s\delta(1-n_p^s) & -c & 0 & 0 \\ uk_s(1-n_{rt}^s)V_s + k_r(1-n_{rt}^r)V_r & 0 & uk_s(1-n_{rt}^s)T & -\delta & k_r(1-n_{rt}^r)T \\ 0 & 0 & 0 & N_r\delta(1-n_p^r) & -c \end{pmatrix}, \tag{10}$$

such that the Jacobian matrix evaluated at the free equilibrium point is

$$J(\xi_1) = \begin{pmatrix} -d - \frac{r}{T_{max}} & 0 & -k_s(1-n_{rt}^s)\frac{\lambda+r}{d+\frac{r}{T_{max}}} & 0 & -k_r(1-n_{rt}^r)\frac{\lambda+r}{d+\frac{r}{T_{max}}} \\ 0 & -\delta & (1-u)k_s(1-n_{rt}^s)\frac{\lambda+r}{d+\frac{r}{T_{max}}} & 0 & 0 \\ 0 & N_s\delta(1-n_p^s) & -c & 0 & 0 \\ 0 & 0 & uk_s(1-n_{rt}^s)\frac{\lambda+r}{d+\frac{r}{T_{max}}} & -\delta & k_r(1-n_{rt}^r)\frac{\lambda+r}{d+\frac{r}{T_{max}}} \\ 0 & 0 & 0 & N_r\delta(1-n_p^r) & -c \end{pmatrix}, \tag{11}$$

$$(J(\xi_1) - \eta I) = \begin{pmatrix} -d - \frac{r}{t_{max}} - \eta & 0 & -k_s(1 - n_r^s) \frac{\lambda+r}{d + \frac{r}{t_{max}}} & 0 & -k_r(1 - n_r^r) \frac{\lambda+r}{d + \frac{r}{t_{max}}} \\ 0 & -\delta - \eta & (1-u)k_s(1 - n_r^s) \frac{\lambda+r}{d + \frac{r}{t_{max}}} & 0 & 0 \\ 0 & N_s\delta(1 - n_p^s) & -c - \eta & 0 & 0 \\ 0 & 0 & uk_s(1 - n_r^s) \frac{\lambda+r}{d + \frac{r}{t_{max}}} & -\delta - \eta & k_r(1 - n_r^r) \frac{\lambda+r}{d + \frac{r}{t_{max}}} \\ 0 & 0 & 0 & N_r\delta(1 - n_p^r) & -c - \eta \end{pmatrix}. \tag{12}$$

The characteristic equation is given as follows:

$$\eta^5 + 53.1\eta^4 + 820.2138\eta^3 + 3101.6195\eta^2 + 4381.3044\eta + 2082.0898 = 0. \tag{13}$$

Then the eigenvalues are given by,

$\eta_1 = -0.0500, \eta_2 = -11.5973, \eta_3 = -0.4027, \eta_4 = -11.6051, \eta_5 = -0.3949$. So, the free equilibrium point for the model is asymptotically stable when $\eta_1, \eta_2, \eta_3, \eta_4$ and $\eta_5 \leq 0$. If all the eigenvalues η_i of the Jacobian matrix $J = \frac{\partial g}{\partial r}$, calculated at the equilibrium point satisfy $|\arg(\eta_i)| > \frac{|\alpha \pm i\beta|\pi}{2}$, and $0 < |\alpha \pm i\beta| \leq 1$ the equilibrium point is locally asymptotically stable.

5 Discretization scheme

Let us consider,

$$t_n = n\Delta t, \quad n = 0, 1, 2, 3, \dots, N_n, \quad h := \Delta t = \frac{t_{final}}{N_n}.$$

Where N_n is a natural number, the final time is t_{final} and h represents the step size.

Numerical values of T, T_s, V_s, T_r and V_r at t_n are denoted by $T_n, T_{sn}, V_{sn}, T_{rn}$ and V_{rn} . Moreover, the Grünwald–Letnikov’s approach for Caputo operator is given as follows:

$${}_0^C D_t^{\alpha \pm i\beta} x(t) |_{t=t_n} = \frac{1}{(\phi(\Delta t)^{\alpha \pm i\beta})} (x_{n+1} - \sum_{i=1}^{n+1} w_i x_{n+1-i} - q_{n+1} x_0), \tag{14}$$

where

$$w_i = (-1)^{i-1} \binom{\alpha \pm i\beta}{i}, \quad w_1 = \alpha \pm i\beta,$$

$$q_i = \frac{i^{-(\alpha \pm i\beta)}}{\Gamma(1 - (\alpha \pm i\beta))}, \quad i = 1, 2, 3, \dots, N_n + 1.$$

Using 14 we can write (7) as follows

$$\begin{aligned}
& \frac{0.5}{(\phi(h))^{\alpha+i\beta}} (T_{n+1} - \sum_{i=1}^{n+1} w_i T_{n+1-i} - q_{n+1} T(0)) + \frac{0.5}{(\phi(h))^{\alpha-i\beta}} (T_{n+1} - \sum_{i=1}^{n+1} w_i^* T_{n+1-i} - q_{n+1}^* T(0)) \\
& \quad = \lambda - dT_{n+1} + r(1 - \frac{T_{n+1}}{T_{max}}) - k_s(1 - n_{rt}^s) V_s T_{n+1} - k_r(1 - n_{rt}^r) V_r T_{n+1}, \\
& \frac{0.5}{(\phi(h))^{\alpha+i\beta}} (T_{s_{n+1}} - \sum_{i=1}^{n+1} w_i T_{s_{n+1}-i} - q_{n+1} T_s(0)) + \frac{0.5}{(\phi(h))^{\alpha-i\beta}} (T_{s_{n+1}} - \sum_{i=1}^{n+1} w_i^* T_{s_{n+1}-i} - q_{n+1}^* T_s(0)) \\
& \quad = (1-u)k_s(1 - n_{rt}^s) V_s T_{n+1} - \delta T_{s_{n+1}}, \\
& \frac{0.5}{(\phi(h))^{\alpha+i\beta}} (V_{s_{n+1}} - \sum_{i=1}^{n+1} w_i V_{s_{n+1}-i} - q_{n+1} V_s(0)) + \frac{0.5}{(\phi(h))^{\alpha-i\beta}} (V_{s_{n+1}} - \sum_{i=1}^{n+1} w_i^* V_{s_{n+1}-i} - q_{n+1}^* V_s(0)) \\
& \quad = N_s \delta(1 - n_p^s) T_{s_{n+1}} - c V_{s_{n+1}}, \\
& \frac{0.5}{(\phi(h))^{\alpha+i\beta}} (T_{r_{n+1}} - \sum_{i=1}^{n+1} w_i T_{r_{n+1}-i} - q_{n+1} T_r(0)) + \frac{0.5}{(\phi(h))^{\alpha-i\beta}} (T_{r_{n+1}} - \sum_{i=1}^{n+1} w_i^* T_{r_{n+1}-i} - q_{n+1}^* T_r(0)) \\
& \quad = uk_s(1 - n_{rt}^s) V_s T_{n+1} + k_r(1 - n_{rt}^r) V_r T_{n+1} - \delta T_{r_{n+1}}, \\
& \frac{0.5}{(\phi(h))^{\alpha+i\beta}} (V_{r_{n+1}} - \sum_{i=1}^{n+1} w_i V_{r_{n+1}-i} - q_{n+1} V_r(0)) + \frac{0.5}{(\phi(h))^{\alpha-i\beta}} (V_{r_{n+1}} - \sum_{i=1}^{n+1} w_i^* V_{r_{n+1}-i} - q_{n+1}^* V_r(0)) \\
& \quad = N_r \delta(1 - n_{rt}^r) T_{r_{n+1}} - c V_{r_{n+1}}. \tag{15}
\end{aligned}$$

Since each of these equations is linear in T_{n+1} , $T_{s_{n+1}}$, $V_{s_{n+1}}$, $T_{r_{n+1}}$ and $V_{r_{n+1}}$. Then some calculations give us the following explicit expressions

$$\begin{aligned}
T_{n+1} &= \frac{1}{\frac{0.5}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5}{(\phi(h))^{\alpha-i\beta}} + d + \frac{r}{T_{max}} + k_s(1 - n_{rt}^s) V_s + k_r(1 - n_{rt}^r) V_r} (\lambda + r + \frac{0.5 \sum_{i=1}^{n+1} w_i T_{n+1-i}}{(\phi(h))^{\alpha+i\beta}} \\
& \quad + \frac{0.5 q_{n+1} T(0)}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5 \sum_{i=1}^{n+1} w_i^* T_{n+1-i}}{(\phi(h))^{\alpha-i\beta}} + \frac{0.5 q_{n+1}^* T(0)}{(\phi(h))^{\alpha-i\beta}}), \\
T_{s_{n+1}} &= \frac{1}{\frac{0.5}{(\phi(h))^{\alpha-i\beta}} + \frac{0.5}{(\phi(h))^{\alpha+i\beta}} + \delta} ((1-u)k_s(1 - n_{rt}^s) V_s T_{n+1} + \frac{0.5 \sum_{i=1}^{n+1} w_i T_{s_{n+1}-i}}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5 \sum_{i=1}^{n+1} w_i^* T_{s_{n+1}-i}}{(\phi(h))^{\alpha-i\beta}} \\
& \quad + \frac{0.5 q_{n+1} T_s(0)}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5 q_{n+1}^* T_s(0)}{(\phi(h))^{\alpha-i\beta}}), \\
V_{s_{n+1}} &= \frac{1}{\frac{0.5}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5}{(\phi(h))^{\alpha-i\beta}} + c} (N_s \delta(1 - n_p^s) T_{s_{n+1}} + \frac{0.5 \sum_{i=1}^{n+1} w_i V_{s_{n+1}-i}}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5 \sum_{i=1}^{n+1} w_i^* V_{s_{n+1}-i}}{(\phi(h))^{\alpha-i\beta}} \\
& \quad + \frac{0.5 q_{n+1}^* V_s(0)}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5 q_{n+1} V_s(0)}{(\phi(h))^{\alpha-i\beta}}), \\
T_{r_{n+1}} &= \frac{1}{\frac{0.5}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5}{(\phi(h))^{\alpha-i\beta}} + \delta} (uk_s(1 - n_{rt}^s) V_s T_{n+1} + k_r(1 - n_{rt}^r) V_r T_{n+1} + \frac{0.5 \sum_{i=1}^{n+1} w_i V_{r_{n+1}-i}}{(\phi(h))^{\alpha+i\beta}} \\
& \quad + \frac{0.5 \sum_{i=1}^{n+1} w_i^* T_{r_{n+1}-i}}{(\phi(h))^{\alpha-i\beta}} + \frac{0.5 q_{n+1} T_r(0)}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5 q_{n+1}^* T_r(0)}{(\phi(h))^{\alpha-i\beta}}), \\
V_{r_{n+1}} &= \frac{1}{\frac{0.5}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5}{(\phi(h))^{\alpha-i\beta}} + c} (N_r \delta(1 - n_{rt}^r) T_{r_{n+1}} + \frac{0.5 \sum_{i=1}^{n+1} w_i V_{r_{n+1}-i}}{(\phi(h))^{\alpha+i\beta}} + \frac{0.5 \sum_{i=1}^{n+1} w_i^* V_{r_{n+1}-i}}{(\phi(h))^{\alpha-i\beta}} + \\
& \quad \frac{0.5 q_{n+1}^* V_r(0)}{(\phi(h))^{\alpha-i\beta}} + \frac{0.5 q_{n+1} V_r(0)}{(\phi(h))^{\alpha+i\beta}}). \tag{16}
\end{aligned}$$

5.1 Boundedness and positivity

This subsection analyzes some properties of the proposed approximation scheme (16).

Theorem 1.(Positivity) Suppose that $T_0 \geq 0, T_{s_0}(0), V_{s_0} \geq 0, T_{r_0} \geq 0$ and $V_{r_0} \geq 0$, then $\phi(h)T_n \geq 0, T_{s_n} \geq 0, V_{s_n} \geq 0, T_{r_n} \geq 0$ and $V_{r_n} \geq 0$ is satisfied, $n = 1, 2, 3, \dots, N_n$.

Proof. Using induction principle, $n = 0$ in (16) :

$$T_1 = \frac{1}{\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + d + \frac{r}{T_{max}} + k_s(1-n_{rt}^s)V_s + k_r(1-n_{rt}^r)V_r} (\lambda + r + \frac{0.5w_i T_0}{\phi(h)^{\alpha+i\beta}} + \frac{0.5q_{n+1}T(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5w_i^* T_0}{\phi(h)^{\alpha-i\beta}} + \frac{0.5q_{n+1}^* T(0)}{\phi(h)^{\alpha-i\beta}}) \geq 0,$$

$$T_{s_1} = \frac{1}{\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + \delta} ((1-u)k_s(1-n_{rt}^s)V_s T_1 + \frac{0.5w_i T_{s_0}}{\phi(h)^{\alpha+i\beta}} + \frac{0.5w_i^* T_{s_0}}{\phi(h)^{\alpha-i\beta}} + \frac{0.5q_{n+1}T_s(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5q_{n+1}^* T_s(0)}{\phi(h)^{\alpha-i\beta}}) \geq 0,$$

$$V_{s_1} = \frac{1}{\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + c} (N_s \delta(1-n_p^s)T_{s_1} + \frac{0.5w_i V_{s_0}}{\phi(h)^{\alpha+i\beta}} + \frac{0.5w_i^* V_{s_0}}{\phi(h)^{\alpha-i\beta}} + \frac{0.5q_{n+1}V_s(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5q_{n+1}^* V_s(0)}{\phi(h)^{\alpha-i\beta}}) \geq 0,$$

$$T_{r_1} = \frac{1}{\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + \delta} (uk_s(1-n_{rt}^s)V_s T_1 + k_r(1-n_{rt}^r)V_r T_{n+1} + \frac{0.5w_i V_{r_0}}{\phi(h)^{\alpha+i\beta}} + \frac{0.5w_i^* V_{r_0}}{\phi(h)^{\alpha-i\beta}} + \frac{0.5q_{n+1}T_r(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5q_{n+1}^* T_r(0)}{\phi(h)^{\alpha-i\beta}}) \geq 0,$$

$$V_{r_1} = \frac{1}{\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + c} (N_r \delta(1-n_{rt}^r)T_{r_1} + \frac{0.5w_i V_{r_0}}{\phi(h)^{\alpha+i\beta}} + \frac{0.5w_i^* V_{r_0}}{\phi(h)^{\alpha-i\beta}} + \frac{0.5q_{n+1}V_r(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5q_{n+1}^* V_r(0)}{\phi(h)^{\alpha-i\beta}}) \geq 0.$$

Since the parameters are positive. Suppose that for all $n < n + 1$ that $T \geq 0, T_s \geq 0, V_s \geq 0, T_r \geq 0$ and $V_r \geq 0$, thus for $n + 1$

$$\begin{aligned} T_{n+1} &= \frac{1}{\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + d + \frac{r}{T_{max}} + k_s(1-n_{rt}^s)V_s + k_r(1-n_{rt}^r)V_r} (\lambda + r + \frac{0.5 \sum_{i=1}^{n+1} w_i T_{n+1-i}}{\phi(h)^{\alpha+i\beta}} \\ &\quad + \frac{0.5q_{n+1}T(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 \sum_{i=1}^{n+1} w_i^* T_{n+1-i}}{\phi(h)^{\alpha-i\beta}} + \frac{0.5q_{n+1}^* T(0)}{\phi(h)^{\alpha-i\beta}}), \\ T_{s_{n+1}} &= \frac{1}{\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + \delta} ((1-u)k_s(1-n_{rt}^s)V_s T_{n+1} + \frac{0.5 \sum_{i=1}^{n+1} w_i T_{s_{n+1-i}}}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 \sum_{i=1}^{n+1} w_i^* T_{s_{n+1-i}}}{\phi(h)^{\alpha-i\beta}} \\ &\quad + \frac{0.5q_{n+1}T_s(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5q_{n+1}^* T_s(0)}{\phi(h)^{\alpha-i\beta}}), \\ V_{s_{n+1}} &= \frac{1}{\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + c} (N_s \delta(1-n_p^s)T_{s_{n+1}} + \frac{0.5 \sum_{i=1}^{n+1} w_i V_{s_{n+1-i}}}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 \sum_{i=1}^{n+1} w_i^* V_{s_{n+1-i}}}{\phi(h)^{\alpha-i\beta}} \\ &\quad + \frac{0.5q_{n+1}V_s(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5q_{n+1}^* V_s(0)}{\phi(h)^{\alpha-i\beta}}), \\ T_{r_{n+1}} &= \frac{1}{\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + \delta} (uk_s(1-n_{rt}^s)V_s T_{n+1} + k_r(1-n_{rt}^r)V_r T_{n+1} + \frac{0.5 \sum_{i=1}^{n+1} w_i V_{r_{n+1-i}}}{\phi(h)^{\alpha+i\beta}} \\ &\quad + \frac{0.5 \sum_{i=1}^{n+1} w_i^* T_{r_{n+1-i}}}{\phi(h)^{\alpha-i\beta}} + \frac{0.5q_{n+1}T_r(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5q_{n+1}^* T_r(0)}{\phi(h)^{\alpha-i\beta}}), \\ V_{r_{n+1}} &= \frac{1}{\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + c} (N_r \delta(1-n_{rt}^r)T_{r_{n+1}} + \frac{0.5 \sum_{i=1}^{n+1} w_i V_{r_{n+1-i}}}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 \sum_{i=1}^{n+1} w_i^* V_{r_{n+1-i}}}{\phi(h)^{\alpha-i\beta}} \\ &\quad + \frac{0.5q_{n+1}V_r(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5q_{n+1}^* V_r(0)}{\phi(h)^{\alpha-i\beta}}). \end{aligned} \tag{17}$$

Theorem 2.(Boundedness). Let that the initial conditions are $T_0 = 1000$, $T_{s_0} = 1$ and $V_{s_0} = T_{r_0} = V_{r_0} = 0.01$, then T_n , T_{s_n} , V_{s_n} , T_{r_n} and V_{r_n} are bounded, $n = 1, 2, 3, 4, \dots, N_n$.

Proof. System (16) can be written:

$$T_{n+1} \left(\frac{0.5}{\phi(h)^{\alpha-i\beta}} + \frac{0.5}{\phi(h)^{\alpha+i\beta}} + d + \frac{r}{T_{max}} + k_s(1 - n_{rt}^s)V_s + k_r(1 - n_{rt}^r)V_r \right) = \left(\lambda + r + \frac{0.5 \sum_{i=1}^{n+1} w_i T_{n+1-i}}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 \sum_{i=1}^{n+1} w_i^* T_{n+1-i}}{\phi(h)^{\alpha-i\beta}} + \frac{0.5 q_{n+1}^* T(0)}{\phi(h)^{\alpha-i\beta}} + \frac{0.5 q_{n+1} T(0)}{\phi(h)^{\alpha+i\beta}} \right),$$

using induction principle, for $n = 0$, we have:

$$\begin{aligned} & T_1 \left(\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + d + \frac{r}{T_{max}} + k_s(1 - n_{rt}^s)V_s + k_r(1 - n_{rt}^r)V_r \right) \\ &= \left(\lambda + r + \frac{0.5 q_1 T(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 w_1 T(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 q_1^* T(0)}{\phi(h)^{\alpha-i\beta}} + \frac{0.5 w_1^* T(0)}{\phi(h)^{\alpha-i\beta}} \right), \\ & T_1 \left(\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + d + \frac{r}{T_{max}} + k_s(1 - n_{rt}^s)V_s + k_r(1 - n_{rt}^r)V_r \right) \\ &= \left(\lambda + r + \frac{0.5 q_1 T(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 w_1^* T(0)}{\phi(h)^{\alpha-i\beta}} + \frac{0.5 q_1^* T(0)}{\phi(h)^{\alpha-i\beta}} + \frac{0.5 w_1 T(0)}{\phi(h)^{\alpha+i\beta}} \right) = M_1. \end{aligned}$$

So,

$$T_1 \leq M_1, T_{s_1} \leq M_1, V_{s_1} \leq M_1, T_{r_1} \leq M_1, V_{r_1} \leq M_1.$$

For $n = 1$, we have:

$$\begin{aligned} & T_2 \left(\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + d + \frac{r}{T_{max}} + k_s(1 - n_{rt}^s)V_s + k_r(1 - n_{rt}^r)V_r \right) \\ &= \left(\lambda + r + \frac{0.5 \sum_{i=1}^2 w_i T_{2-i}}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 q_2 T(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 \sum_{i=1}^2 w_i^* T_{2-i}}{\phi(h)^{\alpha-i\beta}} + \frac{0.5 q_2^* T(0)}{\phi(h)^{\alpha-i\beta}} \right) \leq \left(\lambda + r + \frac{0.5 q_2 T(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 w_1 T_1}{\phi(h)^{\alpha+i\beta}} \right. \\ & \quad \left. + \frac{0.5 w_1^* T_1}{\phi(h)^{\alpha-i\beta}} + \frac{0.5 q_2^* T(0)}{\phi(h)^{\alpha-i\beta}} \right) = M_2. \end{aligned}$$

So,

$$T_2 \leq M_2, T_{s_2} \leq M_2, V_{s_2} \leq M_2, T_{r_2} \leq M_2, V_{r_2} \leq M_2.$$

For $n = 2$, we have:

$$\begin{aligned} & T_3 \left(\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + \frac{0.5 \sum_{i=1}^3 w_i T_{3-i}}{\phi(h)^{\alpha+i\beta}} + d + \frac{r}{T_{max}} + k_s(1 - n_{rt}^s)V_s + k_r(1 - n_{rt}^r)V_r \right) \\ &= \left(\lambda + r + \frac{0.5 \sum_{i=1}^3 w_i^* T_{3-i}}{\phi(h)^{\alpha-i\beta}} + \frac{0.5 q_3 T(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 q_3^* T(0)}{\phi(h)^{\alpha-i\beta}} \right) \leq \left(\lambda + r + \frac{0.5 w_1 T_2}{\phi(h)^{\alpha+i\beta}} + \frac{0.5 q_3 T(0)}{\phi(h)^{\alpha+i\beta}} \right. \\ & \quad \left. + \frac{0.5 w_1^* T_2}{\phi(h)^{\alpha-i\beta}} + \frac{0.5 q_3^* T(0)}{\phi(h)^{\alpha-i\beta}} \right) = M_3. \end{aligned}$$

So,

$$T_3 \leq M_3, T_{s_3} \leq M_3, V_{s_3} \leq M_3, T_{r_3} \leq M_3, V_{r_3} \leq M_3.$$

For $n = 3$, we have:

$$\begin{aligned}
 & T_4 \left(\frac{0.5}{\phi(h)^{\alpha+i\beta}} + \frac{0.5}{\phi(h)^{\alpha-i\beta}} + d + \frac{r}{T_{max}} + k_s(1 - n_{rt}^s)V_s + k_r(1 - n_{rt}^r)V_r \right) \\
 = & \left(\lambda + r + \frac{0.5q_4T(0)}{\phi(h)^{\alpha+i\beta}} + \frac{0.5\sum_{i=1}^4 w_i T_{4-i}}{\phi(h)^{\alpha+i\beta}} + \frac{0.5\sum_{i=1}^4 w_i^* T_{4-i}}{\phi(h)^{\alpha-i\beta}} + \frac{0.5q_4^*T(0)}{\phi(h)^{\alpha-i\beta}} + \frac{0.5\sum_{i=1}^4 w_i T_{4-i}}{\phi(h)^{\alpha+i\beta}} \right) \leq \left(\lambda + r + \frac{0.5w_1T_3}{\phi(h)^{\alpha+i\beta}} + \frac{0.5q_4T(0)}{\phi(h)^{\alpha+i\beta}} \right. \\
 & \left. + \frac{0.5w_1^*T_3}{\phi(h)^{\alpha-i\beta}} + \frac{0.5q_4^*T(0)}{\phi(h)^{\alpha-i\beta}} \right) = M_4.
 \end{aligned}$$

Thus,

$$T_4 \leq M_4, T_{s_4} \leq M_4, V_{s_4} \leq M_4, T_{r_4} \leq M_4, V_{r_4} \leq M_4.$$

Now we suppose that

$$T_n \leq M_n, T_{s_n} \leq M_n, V_{s_n} \leq M_n, T_{r_n} \leq M_n, V_{r_n} \leq M_n.$$

We claim that:

$$T_{n+1} \leq M_{n+1}, T_{s(n+1)} \leq M_{n+1}, V_{s(n+1)} \leq M_{n+1}, T_{r(n+1)} \leq M_{n+1}, V_{r(n+1)} \leq M_{n+1}.$$

5.2 Stability

Scheme(16) is called asymptotically stable, if there are constants L_1, L_2, L_3, L_4, L_5 as $|z| \rightarrow 1$, such that

$$T_{n+1} \leq L_1, T_{s_{n+1}} \leq L_2, V_{s_{n+1}} \leq L_3, T_{r_{n+1}} \leq L_4, V_{r_{n+1}} \leq L_5.$$

Using theorem of boundedness we can claim that NSFDM (16) is asymptotically stable.

6 Numerical simulations

In the following, NSFDM is introduced to study the fraction complex order model (7). The initial conditions are given as follows : $T(0) = 1000, T_s(0) = 1$ and $V_s(0) = T_r(0) = V_r(0) = 0.01$ and $\phi(h) = 1 - e^{-h}$. Parameter values are given in Table 2, and the simulations are given at different values of α and β . To show that the proposed scheme is efficient, we will take different values for the final time with different values of the time step h . Convergences behavior are reported in Table 3 for the following numerical methods: NSFDM, standard finite difference method (SFDM) and ode45 when $\alpha = 1, \beta = 0$. We can claim from this table that for large h NSFDM is convergent while ode45 and SFDM only converge when h is small. Table 4 reports CPU time when $\alpha = 0.9, \beta = 0.2$, i.e., NSFDM is more efficient than the method which used in [2]. Figure 1 shows how the disease-free equilibrium point changes with growth rate f_1 when $\beta = 0.2$ and $\alpha = 1, 0.7$ respectively. Figure 2 exhibits how the drug-sensitive endemic equilibrium point of (7) changes when $u = 3 \times 10^{-8}, kr = 2.0 \times 10^{-5}, ks = 2.4 \times 10^{-5}, Nr = 2300, \beta = 0.2$ and $\alpha = 0.9, 0.7$ respectively and growth rate f_1 using GEM. Figure 3 shows how the drug-sensitive endemic equilibrium point is changed when $N_s = 4000, N_r = 4800, k_r = 2.0 \times 10^{-5}, k_s = 2.4 \times 10^{-5}, \beta = 0.25$ and $\alpha = 0.8, 0.7$ respectively and growth rate f_1 using NSFDM. Figure 4, shows how endemic equilibrium point of the model (7) changes when $k_r = 2.0 \times 10^{-5}, k_s = 2.4 \times 10^{-5}, \beta = 0.21, \alpha = 0.9$ and growth rate f_1 using NSFDM. Figure 5, manifests how the disease-free equilibrium point of the model (7) changes when $\beta = 0.1$ and $\alpha = 0.9, 0.5$ respectively and growth rate f_2 . Figure 6, shows how the drug resistance endemic equilibrium point of the model (7) changes when $N_s = 4000, N_r = 4800, K_s = 2.4 \times 10^{-5}, K_r = 2.0 \times 10^{-5}, \beta = 0.21, \alpha = 1, 0.8$ respectively and growth rate f_2 .

Table 3: Comparing between NSFDM, SFDM and ode45 when $t_{final} = 1000$ for different values of h , $\alpha = 1$, $\beta = 0$.

h	NSFDM	SFDM	ode45
0.1	Convergent	Convergent	Convergent
1	Convergent	Convergent	Convergent
2	Convergent	Divergent	Divergent
10	Convergent	Divergent	Divergent
20	Convergent	Divergent	Divergent
100	Convergent	Divergent	Divergent

Table 4: The CPU time when $\alpha = 0.9$, $\beta = 0.2$.

CPU time for NSFDM	CPU time for [2]
0.3979sec	1.8703 sec
0.4063 sec	2.684614 sec
0.536131 sec	6.715916 sec
0.659607 sec	23.553965 sec

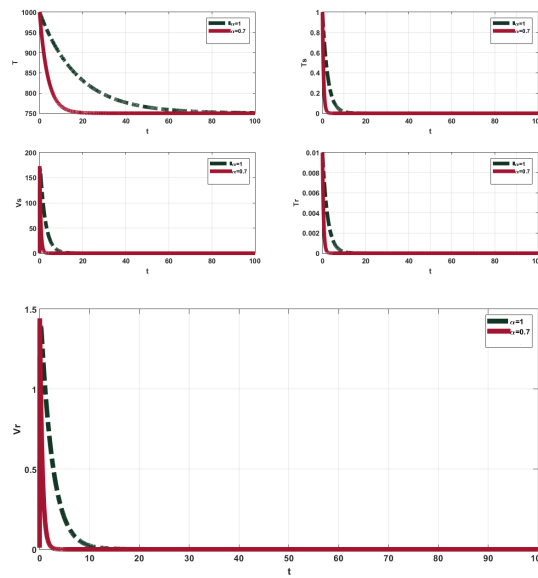


Fig. 1: The disease-free equilibrium point with growth rate f_1 of the model (7) when $\beta = 0.2$.

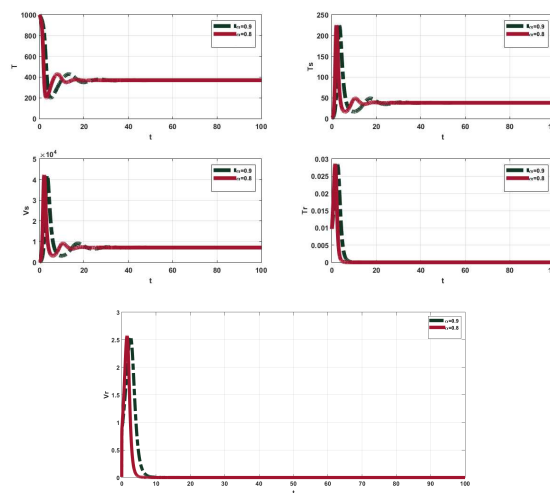


Fig. 2: The endemic equilibrium point of (7) when $\beta = 0.1$ and growth rate f_1 using GEM.

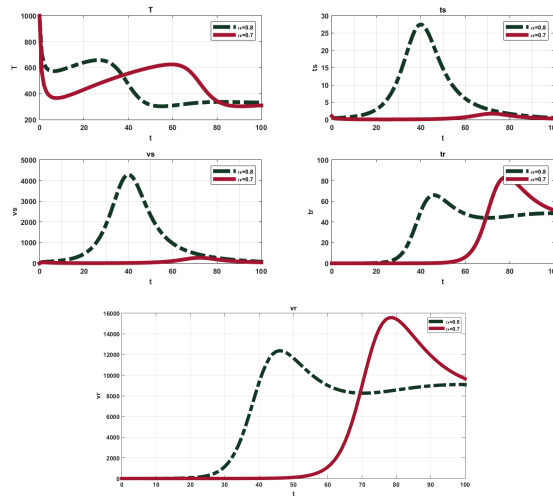


Fig. 3: The endemic equilibrium point with growth rate f_1 of (7) when $\beta = 0.25$ using NSFDM.

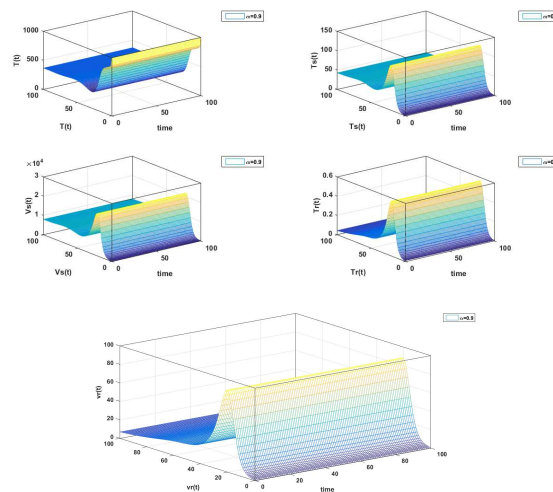


Fig. 4: The endemic equilibrium point with growth rate f_1 of the model (7) when $\beta = 0.21$ using NSFDM.

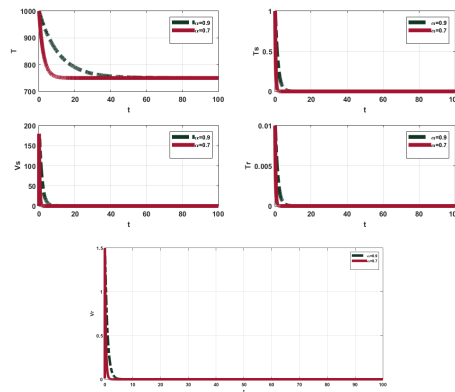


Fig. 5: Growth rate f_2 and disease-free equilibrium point of the model (7) when $\beta = 0.1$.

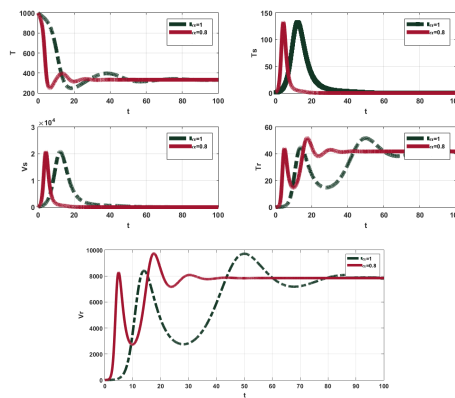


Fig. 6: Endemic equilibrium point of (7) when $\beta = 0.21$ and growth rate f_2 .

7 Conclusion

In this article, the fractional complex order HIV model was numerically investigated. This dynamical model is more suitable to describe the biological phenomena with memory than the fractional and integer order model. In addition, the fractional complex order system reveals rich dynamics and variation of the value of the complex order derivative sheds new light on modeling the intracellular delay. NSFDM has been constructed to simulate the solutions of the proposed model. Some properties of the proposed method, such as positivity and boundedness have been studied numerically. This method has bigger stability region than GEM and Runge-Kutta method. Moreover, NSFDM saves the computational time when the final time is very big and provides valid approximations.

Conflict of Interest

The authors declare that they have no conflict of interest.

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