



Fractional Calculus Model for the Hepatitis C with Different Types of Virus Genome

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Abstract: In this paper, a fractional order model to study the spread of HCV-subtype 4a amongst the Egyptian population is constructed. The stability of the boundary and positive fixed points is studied. The generalized Adams-Bashforth-Moulton method is used to solve and simulate the system of fractional differential equations.

Keywords: Hepatitis C Virus, Fractional Order, Stability, Numerical Method, Sovaldi

1. Introduction

Egypt has possibly the highest HCV prevalence in the world; 10-20% of the general population are infected and HCV is the leading cause of HCC and chronic liver disease in the country [17]. The genomes of HCV display significant sequence heterogeneity and have been classified into types and subtypes. Six types from 1 to 6 have been recognized, each type having a different number of subtypes like a, b, c, etc. Recently, new variants have been identified and assigned to proposed types 7-11. The worldwide presence of the virus and the geographic distribution of genotypes clearly indicate that HCV is an old companion of human kind [20].

Moneim and Mosa [17], constructed a mathematical model to study the spread of HCV-subtype 4a amongst the Egyptian population, we assume that people from the Egyptian population have some factors which lead to substitutions or mutations of the different genotypes of HCV into HCV-subtype 4a. They analyzed and solved the model to derive new results about the behavior of the spread of HCV. In recent decades, the fractional calculus and Fractional differential equations have attracted much attention and increasing interest due to their potential applications in science and engineering [5, 14, 18]. In this paper, we consider the fractional order model for hepatitis C virus and antiviral medication (Sovaldi). We give a detailed analysis for the

asymptotic stability of the model. Adams-Bashforth-Moulton algorithm have been used to solve and simulate the system of differential equations.

2. Model for Mulation

The SI_1I_2R model for the spread of virus HCV-subtype 4a can be written as a set of four coupled nonlinear ordinary differential equations as follows [17]:

$$\begin{aligned}\frac{dS}{dt} &= -(k_1I_1 + k_2I_2)S - bS + A, \\ \frac{dI_1}{dt} &= k_1SI_1 - bI_1 + \mu I_2 - \gamma I_1, \\ \frac{dI_2}{dt} &= k_2SI_2 - bI_2 - \mu I_2 - \delta I_2, \\ \frac{dR}{dt} &= \gamma I_1 + \delta I_2 - bR,\end{aligned}\quad (1)$$

Where

1. R denote the densities (or fractions) of recovered individuals.
2. The birth rate is equal a positive constant rate (c), and death rate is equal a positive constant rate (b),
3. γ , δ be the rate at which susceptible individuals a removed after taking the medicine from I_1 , I_2 , respectively.

The population is mixing in a homogenous manner, i.e. every person has the same chance of coming in contact with an infected person.

Where $\gamma, \delta \geq 0$ and all the other parameters are positive. If $\gamma = \delta = 0$, which means there are no cure by treatment, then $\lim_{t \rightarrow \infty} I_1(t) = \lim_{t \rightarrow \infty} I_2(t) = 0$. System (1) will reduce to the standard SR model.

Fractional order models are more accurate than integer-order models as fractional order models allow more degrees of freedom. Fractional differential equations also serve as an excellent tool for the description of hereditary properties of various materials and processes. The presence of memory term in such models not only takes into account the history of the process involved but also carries its impact to present and future development of the process. Fractional differential equations are also regarded as an alternative model to nonlinear differential equations. In consequence, the subject of fractional differential equations is gaining much importance and attention. For some recent work on fractional differential equations, see [5, 14, 18]. Now we introduce fractional order in to the ODE model by Liu et al. [16]. The new system is described by the following set of fractional order differential equations:

$$\begin{aligned} D_t^\alpha S &= -(k_1 I_1 + k_2 I_2)S - bS + A, \\ D_t^\alpha I_1 &= k_1 S I_1 - b I_1 + \mu I_2 - \gamma I_1, \\ D_t^\alpha I_2 &= k_2 S I_2 - b I_2 - \mu I_2 - \delta I_2, \\ D_t^\alpha R &= \gamma I_1 + \delta I_2 - b R, \end{aligned} \quad (2)$$

where D_t^α is the Caputo fractional derivative and $A=cN$. Because model (2) monitors the dynamics of human populations, all the parameters are assumed to be non-negative. Furthermore, it can be shown that all state variables of the model are non-negative for all time $t \geq 0$ (see, for instance, [4, 10]).

Lemma 1 The closed set $\Omega = \{(S, I_1, I_2, R) \in R_+^4: S + I_1 + I_2 + R = 1\}$ is positively invariant with respect to model (2).

Proof. The fractional derivative of the total population, obtained by adding all the equations of model (2), is given by

$$D_t^\alpha N(t) = A - bN(t) \quad (3)$$

The solution to Eq. (3) is given by

$$N(t) = N(0)E_{\alpha,1}(-bt^\alpha) + At^\alpha E_{\alpha,\alpha+1}(-bt^\alpha) \quad (4)$$

where $E_{\alpha,1}$ is the Mittag-Leffler function. Therefore, all solutions of the model with initial conditions in Ω remain in Ω for all $t > 0$. Thus, region Ω is positively invariant with respect to model (2).

In the following, we will study the dynamics of system (2).

3. Equilibrium Point and Stability

In the following, we discuss the stability of the commensurate fractional ordered dynamical system:

$$D_t^\alpha x_i = f_i(x_1, x_2, x_3), \quad \alpha \in (0,1), \quad 1 \leq i \leq 3 \quad (5)$$

Let $E = (x_1^*, x_2^*, x_3^*)$ be an equilibrium point of system (3.1) and $x_i = x_i^* + \eta_i$, where η_i is a small disturbance from a fixed point. Then

$$\begin{aligned} D_t^\alpha \eta_i &= D_t^\alpha x_i \\ &= f_i(x_1^* + \eta_1, x_2^* + \eta_2, x_3^* + \eta_3) \\ &\approx \eta_1 \frac{\partial f_i(E)}{\partial x_1} + \eta_2 \frac{\partial f_i(E)}{\partial x_2} + \eta_3 \frac{\partial f_i(E)}{\partial x_3} \end{aligned} \quad (6)$$

System (6) can be written as:

$$D_t^\alpha \eta = J\eta \quad (7)$$

where $\eta = (\eta_1, \eta_2, \eta_3)^T$ and J is the Jacobian matrix evaluated at the equilibrium points. Using Matignon's results [23], it follows that the linear autonomous system (3.3) is asymptotically stable if $|\arg(\lambda)| > \frac{\alpha\pi}{2}$ is satisfied for all eigenvalues of matrix J at the equilibrium point $E = (x_1^*, x_2^*, x_3^*)$. If $\Phi(x) = x^3 + a_1x^2 + a_2x + a_3$, Let $D(\Phi)$ denote the discriminant of a polynomial Φ , then

$$\begin{aligned} D(\Phi) &= - \begin{vmatrix} 1 & a_1 & a_2 & a_3 & 0 \\ 0 & 1 & a_1 & a_2 & a_3 \\ 3 & 2a_1 & a_2 & 0 & 0 \\ 0 & 3 & 2a_1 & a_2 & 0 \\ 0 & 0 & 3 & 2a_1 & a_2 \end{vmatrix} \\ &= 18a_1a_2a_3 + (a_1a_2)^2 - 4a_3a_1^3 - 4a_2^3 \\ &\quad - 27a_3^2. \end{aligned}$$

Following [1, 2, 3, 15], we have the proposition.

Proposition 3.1 One assumes that E exists in R_+^3 .

1. If the discriminant of $\Phi(x)$, $D(\Phi)$ is positive and Routh-Hurwitz are satisfied, that is, $D(\Phi) > 0$, $a_1 > 0$, $a_3 > 0$, $a_1a_2 > a_3$, then E is locally asymptotically stable.

2. If $D(\Phi) < 0$, $a_1 > 0$, $a_2 > 0$, $a_1a_2 = a_3$, $\alpha \in [0,1)$ then E is locally asymptotically stable.

3. If $D(\Phi) < 0$, $a_1 < 0$, $a_2 < 0$, $\alpha > \frac{2}{3}$, then E is unstable.

4. The necessary condition for the equilibrium point E , to be locally asymptotically stable, is $a_3 > 0$.

To evaluate the equilibrium points, let

$$D_t^\alpha S = 0, \quad D_t^\alpha I_1 = 0, \quad D_t^\alpha I_2 = 0, \quad D_t^\alpha R = 0.$$

Then

1. the first disease free equilibrium (DFE) point is $E_0 = (S_0, I_{10}, I_{20}, R_0) = (\frac{A}{b}, 0, 0, 0)$, when the disease is absent in the population, in this case ($I_1 = I_2 = 0$), therefore the population is fully susceptible.

The basic reproductive number R_0 is defined as the expected number of secondary cases produced by a single infected individual entering the population at the DFE [5]. It means the average new infections produced by one infected individual during his lifespan when the population is at E_0 .

Theorem 3.2 For the system (1) one have the basic reproduction number

$$R_0 = \max \left[\frac{k_1 A}{b(b + \gamma)}, \frac{k_2 A}{b(b + \mu + \delta)} \right]$$

Proof We will use the next generation method to find the basic reproduction number, for the system (1), rewrite the equations by which classes infection first and then the rest of the equations secondly, we have

$$\begin{aligned} \frac{dI_1}{dt} &= k_1 S I_1 - b I_1 + \mu I_2 - \gamma I_1, \\ \frac{dI_2}{dt} &= k_2 S I_2 - b I_2 - \mu I_2 - \delta I_2, \\ \frac{dS}{dt} &= -(k_1 I_1 + k_2 I_2) S - b S + A, \\ \frac{dR}{dt} &= \gamma I_1 + \delta I_2 - b R, \end{aligned} \quad (8)$$

We make matrices f, v , such that the system (8) in the form

$$\frac{dX}{dt} = f(x) - v(x),$$

Where

$$f(x) = \begin{bmatrix} f_1 \\ f_2 \\ f_3 \\ f_4 \end{bmatrix} = \begin{bmatrix} k_1 S I_1 \\ k_2 S I_2 \\ 0 \\ 0 \end{bmatrix},$$

$$v(x) = \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \end{bmatrix} = \begin{bmatrix} b I_1 - \mu I_2 + \gamma I_1 \\ (b + \mu + \delta) I_2 \\ (k_1 I_1 + k_2 I_2) S + b S - A \\ -\gamma I_1 - \delta I_2 + b R \end{bmatrix}$$

We make matrices F, V , such that

$$F(x) = \begin{bmatrix} \frac{\partial f_1}{\partial I_1} & \frac{\partial f_1}{\partial I_2} \\ \frac{\partial f_2}{\partial I_1} & \frac{\partial f_2}{\partial I_2} \end{bmatrix}, V(x) = \begin{bmatrix} \frac{\partial v_1}{\partial I_1} & \frac{\partial v_1}{\partial I_2} \\ \frac{\partial v_2}{\partial I_1} & \frac{\partial v_2}{\partial I_2} \end{bmatrix}$$

then

$$F(x) = \begin{bmatrix} k_1 S & 0 \\ 0 & k_2 S \end{bmatrix}, V(x) = \begin{bmatrix} b + \gamma & -\mu \\ 0 & b + \mu + \delta \end{bmatrix},$$

at the first disease free equilibrium (DFE) point $E_0 = (\frac{A}{b}, 0, 0, 0)$ the matrix F become

$$F(x) = \begin{bmatrix} \frac{k_1 A}{b} & 0 \\ 0 & \frac{k_2 A}{b} \end{bmatrix},$$

we now find the inverse matrix V^{-1} of V

$$V^{-1} = \begin{bmatrix} \frac{1}{b + \gamma} & \frac{\mu}{(b + \gamma)(b + \mu + \delta)} \\ 0 & \frac{k_2 A}{b + \mu + \delta} \end{bmatrix},$$

we need to find the multiplying $F \cdot V^{-1}$, we have

$$F \cdot V^{-1} = \begin{bmatrix} \frac{k_1 A}{b(b + \gamma)} & \frac{k_1 A \mu}{b(b + \gamma)(b + \mu + \delta)} \\ 0 & \frac{k_2 A}{b(b + \mu + \delta)} \end{bmatrix},$$

to get the eigenvalues of $F \cdot V^{-1}$ we solve the equation

$$|F \cdot V^{-1} - \lambda I| = 0 \quad (9)$$

where λ is the eigenvalues and I is the identity matrix, we have

$$\begin{vmatrix} \frac{k_1 A}{b(b + \gamma)} - \lambda & \frac{k_1 A \mu}{b(b + \gamma)(b + \mu + \delta)} \\ 0 & \frac{k_2 A}{b(b + \mu + \delta)} - \lambda \end{vmatrix} = 0,$$

then

$$\lambda_1 = \frac{k_1 A}{b(b + \gamma)}, \quad \lambda_2 = \frac{k_2 A}{b(b + \mu + \delta)}.$$

where $F \cdot V^{-1}$ is the next generation matrix for the model (1). It follows that the spectral radius of matrix $F \cdot V^{-1}$ is

$$\rho(F \cdot V^{-1}) = \max(\lambda_i), i = 1, 2.$$

$$\text{Then } R_0 = \max \left[\frac{k_1 A}{b(b + \gamma)}, \frac{k_2 A}{b(b + \mu + \delta)} \right].$$

Let $R_{01} = \frac{k_1 A}{b(b + \gamma)}$, $R_{02} = \frac{k_2 A}{b(b + \mu + \delta)}$, then

2. By (2), a positive equilibrium point $E_1 = (S_1, I_{11}, I_{21}, R_1) = \left(\frac{b + \gamma}{k_1}, \frac{b}{k_1} (R_{01} - 1), 0, \frac{\gamma}{k_1} (R_{01} - 1) \right)$, which is the free HCV infection from all types except 4a ($I_{21} = 0$).

3. The third point is the endemic from all types of infection. Then ($I_1 \neq 0 \neq I_2$). Therefore the third equilibrium point is $E_2 = (\frac{A}{R_{02}}, I_{12}, I_{22}, R_2)$ where

$$I_{12} = \frac{b \mu (R_{02} - 1)}{k_2 (b + \delta) - k_1 (b + \gamma)},$$

$$I_{22} = \frac{I_{12}}{\mu k_2} \left(\frac{R_{02}}{R_{01}} - 1 \right),$$

$$R_2 = \left[\frac{\delta}{b \mu k_2 (b + \mu + \delta)} \left(\frac{R_{02}}{R_{01}} - 1 \right) + \frac{\gamma}{b} \right] I_{12}.$$

Remark. The free HCV type 4a infection, ($I_1 = 0$ and $I_2 = +ev$), does not exist, as there is a positive mutation rate μ from infective class, I_2 , to infective class, I_1 , so if $I_1 = 0$ then it should be that, $I_2 = 0$ is the (DFE) again.

The Jacobian matrix $J(E_0)$ for system given in (2) evaluated at the disease free equilibrium is as follows:

$$J(E_0) = \begin{pmatrix} -b & -(b+\gamma)R_{01} & -(b+\mu+\delta)R_{02} & 0 \\ 0 & (b+\gamma)(R_{01}-1) & \mu & 0 \\ 0 & 0 & (b+\mu+\delta)(R_{02}-1) & 0 \\ 0 & \gamma & \delta & -b \end{pmatrix}$$

Theorem 3.3 The disease free equilibrium E_0 is locally asymptotically stable if $\max(R_{01}, R_{02}) < 1$ and is unstable if at least one of $(R_{01}, R_{02}) > 1$.

Proof. The disease free equilibrium is locally asymptotically stable if all the eigenvalues, $\lambda_{0i}, i = 1, 2, 3, 4$ of the Jacobian matrix $J(E_0)$ satisfy the following condition [1, 2, 3, 8, 11, 17]:

$$|\arg(\lambda_{0i})| > \frac{\pi}{2} \quad (10)$$

The eigenvalues of the characteristic equation of $J(E_0)$ are $\lambda_{01} = -b, \lambda_{02} = (b+\gamma)(R_{01}-1), \lambda_{03} = (b+\mu+\delta)(R_{02}-1)$ and $\lambda_{04} = -b$. Hence E_0 is locally asymptotically stable if $\max(R_{01}, R_{02}) < 1$ and is unstable if at least one of $(R_{01}, R_{02}) > 1$.

We now discuss the asymptotic stability of a positive equilibrium point E_1 of the system given by (2). The Jacobian matrix $J(E_1)$ evaluated at a positive equilibrium is given as:

$$J(E_1) = \begin{pmatrix} -b(R_{01}-1)-b & -(b+\gamma) & -\frac{k_2(b+\gamma)}{k_1} & 0 \\ b(R_{01}-1) & 0 & \mu & 0 \\ 0 & 0 & (b+\mu+\delta)\left(\frac{R_{02}}{R_{01}}-1\right) & 0 \\ 0 & \gamma & \delta & -b \end{pmatrix}$$

The eigenvalues of the characteristic equation of $J(E_1)$ are $\lambda_{11} = -b, \lambda_{12} = (b+\mu+\delta)\left(\frac{R_{02}}{R_{01}}-1\right)$ and

$$J(E_2) = \begin{pmatrix} -bR_{02} & -(b+\gamma)\frac{R_{01}}{R_{02}} & -(b+\mu+\delta) & 0 \\ \frac{b\mu k_1(R_{02}-1)}{k_2(b+\gamma)-k_1(b+\delta)} & (b+\gamma)\left(\frac{R_{01}}{R_{02}}-1\right) & \mu & 0 \\ \frac{k_2(b+\gamma)(R_{01}-R_{02})(R_{02}-1)}{R_{02}[k_1(b+\delta)-k_2(b+\gamma)]} & 0 & 0 & 0 \\ 0 & \gamma & \delta & -b \end{pmatrix}$$

The characteristic equation of $J(E_2)$ is

$$(\lambda + b)(\lambda^3 + A\lambda^2 + B\lambda + C) = 0$$

Where

$$A = bR_{02} - (b+\gamma)\left(\frac{R_{01}}{R_{02}}-1\right),$$

$$B = \frac{(b+\gamma)}{R_{02}[k_2(b+\gamma)-k_1(b+\delta)]} \{b^2R_{02}(R_{01}-R_{02})(k_1-k_2) + R_{02}^2(k_2(\gamma+1)-k_1\delta) + R_{02}[k_1R_{01}(\mu+\delta)-k_2(R_{01}(\gamma+1)+1)] - bR_{01}(\mu k_1-k_2) - k_2(R_{02}-1)(R_{01}-R_{02})(\mu+\delta)\},$$

$$\lambda_{13}, \lambda_{14} = -\frac{b}{2}R_{01} \pm \sqrt{\frac{b^2}{4}R_{01}^2 + b(b+\gamma)(1-R_{01})}.$$

Theorem 3.4 The equilibrium point E_1 is locally asymptotically stable if and only if $1 < R_{02} < R_{01}$.

Proof. We start our proof by assuming that the equilibrium point E_1 is locally asymptotically stable. Then $\lambda_{12} < 0$. Hence,

$$(b+\mu+\delta)\left(\frac{R_{02}}{R_{01}}-1\right) < 0$$

So, $R_{02} < R_{01}$. Conversely, assume that $1 < R_{02} < R_{01}$ and if the equilibrium point E_1 is not locally asymptotically stable, then at least one of the following cases holds

- $\lambda_{12} \geq 0$. Thus $(R_{02} \geq R_{01})$ which is a contradiction.
- λ_{13} is a complex number with nonnegative real part, i.e. $(-\frac{b}{2}R_{01} > 0)$ which is also a contradiction with the fact that $(R_{01} > 0)$.
- λ_{13} is a real number and nonnegative, i.e.

$$-\frac{b}{2}R_{01} \pm \sqrt{\frac{b^2}{4}R_{01}^2 + b(b+\gamma)(1-R_{01})} \geq 0 \Rightarrow$$

$$R_{01} \leq \sqrt{R_{01}^2 + \frac{2(b+\gamma)}{b}(1-R_{01})}.$$

This leads to $R_{01} < 1$ which contradicts with the assumption. Finally, it is obvious that λ_{14} has a negative real part. Therefore we can deduce that, the equilibrium point E_1 is locally asymptotically stable.

We now discuss the asymptotic stability of the endemic (positive) equilibrium point E_2 of the system given by (2). The Jacobian matrix $J(E_2)$ evaluated at a endemic (positive) equilibrium point is given as:

$$C = \frac{k_2(R_{01} - R_{02})(R_{02} - 1)(b + \gamma)^2[R_{01}(b + \delta) - R_{02}(b + \mu + \delta)]}{R_{02}^2[k_2(b + \gamma) - k_1(b + \delta)]}.$$

Following from proposition (1), a necessary condition for $|\arg(\lambda)| > \frac{\alpha\pi}{2}$ is $bC > 0$. Then one has the following theorem:

Theorem 3.5 *The endemic equilibrium point E_2 is locally asymptotically stable if $R_{02} > R_{01} > 1$, and unstable if $R_{02} < R_{01}$. If one take*

$$k_1 = 0.42 \times 10^{-6}, \quad k_2 = 0.164 \times 10^{-5}, \quad b = 0.02, c = 0.01, \quad \mu = 0.02, \quad \gamma = 0.001, \quad \delta = 0.001, \quad N = 1000000$$

It follows that $R_{01} = 10, R_{02} = 20$. In this case, the endemic equilibrium point $E_2 = (25000, 15612.8, 8196.7, 1190.47)$ is local asymptotically stable where the eigenvalues are

$$\lambda_{21} = -0.02,$$

$$\lambda_{22} = -0.1564191,$$

$$\lambda_{23} = -0.197429 + 0.69566I,$$

$$\lambda_{24} = -0.197429 - 0.69566I.$$

4. Numerical Methods and Simulations

Since most of the fractional-order differential equations do not have exact analytic solutions, approximation and numerical techniques must be used. Several analytical and numerical methods have been proposed to solve the fractional order differential equations. For numerical solutions of system (2), one can use the generalized Adams-Bashforth-Moulton method. To give the approximate solution by means of this algorithm, consider the following nonlinear fractional differential equation [6, 7, 15]

$$D_t^\alpha y(t) = f(t, y(t)), \quad 0 \leq t \leq T,$$

$$y^{(k)}(0) = y_0^k, \quad k = 0, 1, 2, \dots, m-1, \quad m-1 < \alpha \leq m,$$

This equation is equivalent to the Volterra integral equation

$$y(t) = \sum_{k=0}^{m-1} y_0^{(k)} \frac{t^k}{k!} + \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} f(s, y(s)) ds. \quad (11)$$

Diethelm et al. used the predictor-correctors scheme [6, 7], based on the Adams-Bashforth-Moulton algorithm to integrate Eq. (4.1). By applying this scheme to the fractional-order model for Hepatitis C virus, and setting $h = \frac{T}{N}, t_n = nh, n = 0, 1, 2, \dots, N \in \mathbb{Z}^+$, Eq. (4.1) can be discretized as follows [6, 7, 15]:

$$S_{n+1} = S_0 + \frac{h^\alpha}{\Gamma(\alpha+2)} \left[-\left(k_1 I_{1(n+1)}^p + k_2 I_{2(n+1)}^p \right) S_{n+1}^p - b S_{n+1}^p + A \right] + \frac{h^\alpha}{\Gamma(\alpha+2)} \sum_{j=1}^n a_{j,n+1} \left[-(k_1 I_{1(j)} + k_2 I_{2(j)}) S_j - b S_j + A \right],$$

$$I_{1(n+1)} = I_{1(0)} + \frac{h^\alpha}{\Gamma(\alpha+2)} \left[k_1 S_{n+1}^p I_{1(n+1)}^p - (b + \gamma) I_{1(n+1)}^p + \mu I_{2(n+1)}^p \right] + \frac{h^\alpha}{\Gamma(\alpha+2)} \sum_{j=1}^n a_{j,n+1} \left[k_1 S_j I_{1(j)} - (b + \gamma) I_{1(j)} + \mu I_{2(j)} \right],$$

$$I_{2(n+1)} = I_{2(0)} + \frac{h^\alpha}{\Gamma(\alpha+2)} \left[k_2 S_{n+1}^p I_{2(n+1)}^p - (b + \mu + \delta) I_{2(n+1)}^p \right] + \frac{h^\alpha}{\Gamma(\alpha+2)} \sum_{j=1}^n a_{j,n+1} \left[k_2 S_j I_{2(j)} - (b + \mu + \delta) I_{2(j)} \right],$$

$$R_{n+1} = R_0 + \frac{h^\alpha}{\Gamma(\alpha+2)} \left[\gamma I_{1(n+1)}^p + \delta I_{2(n+1)}^p - b R_{n+1}^p \right] + \frac{h^\alpha}{\Gamma(\alpha+2)} \sum_{j=1}^n a_{j,n+1} \left[\gamma I_{1(j)} + \delta I_{2(j)} - b R_j \right],$$

where

$$S_{n+1}^p = S_0 + \frac{1}{\Gamma(\alpha)} \sum_{j=0}^n b_{j,n+1} \left[-(k_1 I_{1(j)} + k_2 I_{2(j)}) S_j - b S_j + A \right],$$

$$I_{1(n+1)}^p = I_{1(0)} + \frac{1}{\Gamma(\alpha)} \sum_{j=0}^n b_{j,n+1} \left[k_1 S_j I_{1(j)} - (b + \gamma) I_{1(j)} + \mu I_{2(j)} \right],$$

$$I_{2(n+1)}^p = I_{2(0)} + \frac{1}{\Gamma(\alpha)} \sum_{j=0}^n b_{j,n+1} [k_2 S_j I_{2(j)} - (b + \mu + \delta) I_{2(j)}],$$

$$R_{n+1}^p = R_0 + \frac{1}{\Gamma(\alpha)} \sum_{j=0}^n b_{j,n+1} [\gamma I_{1(j)} + \delta I_{2(j)} - b R_j],$$

$$a_{j,n+1} = \begin{cases} n^{\alpha-1} - (n-\alpha)(n+1) & j=0, \\ (n-j-2)^{\alpha+1} + (n-j)^{\alpha+1} - 2(n-j+1)^{\alpha+1} & 1 \leq j \leq n, \\ 1 & j=n, \end{cases}$$

$$b_{j,n+1} = \frac{h^\alpha}{\alpha} [(n-j+1)^\alpha - (n-j)^\alpha], \quad 0 \leq j \leq n.$$

5. Conclusion

In this paper, we consider the fractional order model for Hepatitis C virus and vaccines. We have obtained a stability condition for equilibrium points. We have also given a numerical example and verified our results. One should note that although the equilibrium points are the same for both integer order and fractional order models, the solution of the fractional order model tends to the fixed point over a longer period of time. One also needs to mention that when dealing with real life problems, the order of the system can be determined by using the collected data. The transformation of a classical model into a fractional one makes it very sensitive to the order of differentiation α : a small change in α may

result in a big change in the final result. From the numerical results Figures follows, it is clear that the approximate solutions depend continuously on the fractional derivative α . The simulation results of our model have been performed using Matlab. We use some documented data for some parameters like death rate $b = 0.02$, birth rate $c = 0.04$ take the number of population $N = 1,000,000$ and then suggest the other parameters such as mutation rate $\mu = 0.02$, the contact rates between S and both of I_1 and I_2 (k_1, k_2) respectively. Finally, the values of the basic reproductive numbers (R_{01}, R_{02}) have been suggested to be first, less than one in value and then larger enough than one to test the stability of the three different equilibrium points of our model.

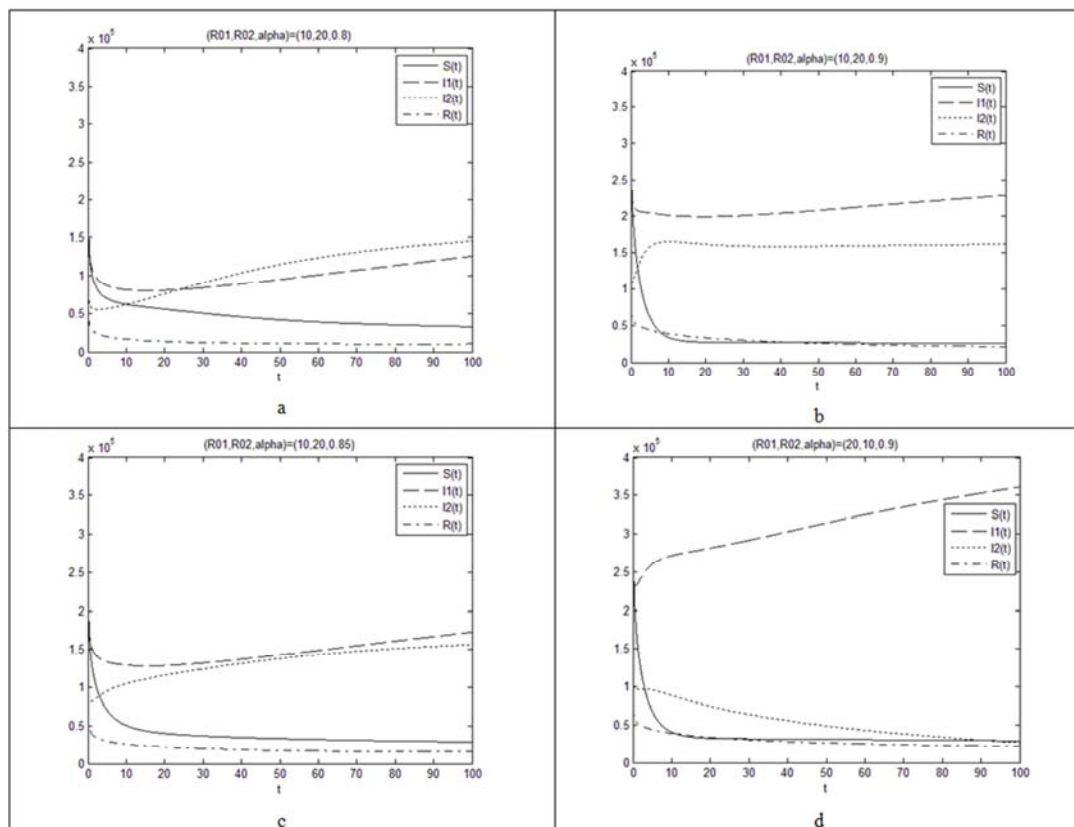


Figure 1. The approximate solutions $S(t), I_1(t), I_2(t)$ and $R(t)$ are displayed in Figs. a-d, respectively. In each figure three different values of (R_{01}, R_{02}, α) .

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