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Application of Elzaki Transform Method for Solving and Interpreting HIV Superinfection Model

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***Abstract*—In this work, a superinfection model of two HIV strains was proposed. The proposed model was solved and interpreted using the Elzaki Transform Method (ETM). The proposed model presented some non-linear terms which are difficult to resolve using the ETM. Hence, we employed the Adomian Decomposition Method (ADM) to resolve the nonlinear terms. We derived an iterative scheme that was used to predict the behavior of the model. Results of data simulation showed that the population of healthy CD4+ T cells declined with respect to time in the presence of HIV strains. The viral loads for both viral strains are observed to be on a steady increase. The study reveals that ETM can be used to solve Superinfection models of HIV. The method is easier, more efficient, and more effective, and it converges faster to the solution when compared to other transform methods. We recommend that ETM can be applied to superinfection and co-infection models of other infectious diseases.**

Keywords— Parameters, Superinfection, Variables, Viral strains

I. Introduction

Acquired Immune Deficiency Syndrome (AIDS) is one of the diseases that have called for collaborating efforts of scientists, modelers, governments, and multinational organizations. The disease is caused by a virus called Human Immunodeficiency Virus (HIV). As the years go by, HIV keeps presenting new dimensions for study. One such area is that HIV has types, sub-types, and sub-subtypes, depending on their genetic composition. About 49 circulating recombinant forms (CRFs) are reported to exist, [1]. Emerging research has shown that an infected person with a viral strain can be re-infected with a unique strain at another time after the establishment of the primary infection. This is what is termed a superinfection, [2].

The possibility of superinfection has been envisaged for many years, but poor and insufficient documentation of samples coupled with techniques for detecting it have constituted major setbacks until 2002 when the first case was reported. Superinfection occurs in several ways. It was reported that transmission takes place in men who have sex with men. Another study revealed superinfection in intravenous drug users, [2], [3]. Superinfection of seropositive wives was also reported by [4].

HIV/AIDS is one of the leading epidemics in the world. About 38 million people globally were living with HIV while 1.7 million people became newly infected with HIV in 2020, [5]. In Africa, more than 20 million people are living with HIV and more than 730,000 new HIV-1 infections still occur each year, [6]. One of the key areas that have become an area of interest to modelers is the fact that viruses have types, forms, and shapes. There are virus trains and each has a unique way of affecting the immune. HIV can be divided into type 1 (HIV-1) and type 2 (HIV-2). Due to variation in the genes of HIV-1, HIV-1 is further divided into groups M (major), O (outlier), and N (non-M, non-O). Within group M, multiple unique subtypes and circulating recombinant forms have been identified, [2], [3].

In [2], the authors proposed an HIV superinfection model of men who have sex with men. Their work focused on the stability analysis of the model. More so, the proposed model in [2], is an in vitro study. Another study, [7], developed superinfection models for bystander killing of uninfected cells, saturating dynamics of new infections, multiple target cell types, and HIV-induced T-cell activation. Analysis of the effects of HIV superinfection was carried out but the model was not solved.

In this work, we propose an in vivo (within-host) model of HIV Superinfection. We aim to solve and interpret the HIV Superinfection model using the Elzaki Transform Method

against the use of other traditional methods such as the Laplace Transform, Taylor's Series, Fourier Transform, and Differential Transform. The behavior of the model was predicted using the iterative scheme that was derived for the model.

II. MODEL DEVELOPMENT AND DESCRIPTION

An infected person with a viral strain can be infected with a unique strain at another time after the establishment of the primary infection. The interest here is to study the behavior of this system in the presence of two viral strains. Thus, an HIV Superinfection deterministic model was proposed in this work. The model comprises five classes dealing with cellular and viral populations. The susceptible population is the uninfected CD4+T cells, U, with source term and natural death rate, s_1 and μ respectively. The two viral strains are denoted by V_p and V_s (which are the primary and superinfection viral strains respectively), with respective natural death rates, μ_p and μ_s. The fourth and the fifth classes are the primarily infected CD4+T cells, I_p and superinfected CD4+T cells, I_s.

A. Basic Assumptions of the HIV Superinfection Model

(i) Viral strains co-exist and co-circulate in the system.
(ii) Superinfection by a distinct viral strain only takes place after the primary establishment of the primary infection by the first strain.

Relying on the description and assumptions of the model above, we present the following expressions as the equations of the model.

$$\frac{dU}{dt} = s_1 - \beta V_p U - \mu U \tag{1}$$

$$\frac{dI_p}{dt} = \beta V_p U - \alpha V_s I_p - \mu_p I_p \tag{2}$$

$$\frac{dI_s}{dt} = \alpha V_s I_p + \mu_s I_s \tag{3}$$

$$\frac{dV_p}{dt} = \mu_p \rho N_p I + \mu_s (1-\gamma) N_s I_s - \beta V_p U - \delta_p V_p \tag{4}$$

$$\frac{dV_s}{dt} = \mu_s \gamma N_s I_s - \delta_p V_s I_p - \delta_s V_s \tag{5}$$

A description of the variables is presented in Table I. Similarly, a description of the parameters is presented in Table II.

TABLE I. DESCRIPTION OF VARIABLES

Symbols	Variables
U	Population of uninfected CD4+T cells
I_p	Population of CD4+T cells infected by viral strain 1
I_s	Population of CD4+T cells infected by viral strain 2
V_p	Population of viral strain 1
V_s	Population of viral strain 2
N_p	Number of viruses produced due to lysing of infected cells by the viral strain
N_s	Number of viruses produced due to lysing of infected cells by viral strain 2

TABLE II. DESCRIPTION OF PARAMETERS

Symbols	Description
s_1	Source term for uninfected CD4+T cells
μ	Natural death rate of uninfected CD4+T cells
μ_p	Natural death rate of CD4+T cells infected by viral strain 1
μ_s	Natural death rate of CD4+T cells infected by viral strain 2
δ_p	Natural death rate of viral strain 1
δ_s	Natural death rate of viral strain 2
β	Rate at which uninfected CD4+T cells are infected by viral strain 1
α	Rate at which primarily infected CD4+T cells are infected by viral strain 2
ρ	Rate at which viruses are produced from CD4+T cells infected by viral strain 1
γ	Rate at which viruses are produced from CD4+T cells infected by viral strain 2

III. THE ELZAKI TRANSFORM METHOD

The Elzaki Transform Method (ETM) was proposed by [8]. The method can be used to solve both ordinary differential equations and partial differential equations. It is effective in deriving solutions of higher-order linear ordinary differential equations. It is an integral transform with a resemblance to the Laplace Transform, [9], [10]. Elzaki Transforms has united preserving properties. Thus, it is not necessary to resort to the frequency domain of a problem before applying the ETM to it. This is one of the merits of the ETM over other transforms. Furthermore, the method preserves the property of linearity, for it is itself linear. The solution obtained using this technique is expressed as an infinite series, [11].

The ETM however has a demerit. It is not designed to handle difficulties that could be posed by nonlinear terms, hence the introduction of a decomposition method to decompose the nonlinear terms, [9]. We employed the Adomian Decomposition Method (ADM) to decompose the nonlinear terms in the model equations, [12].

The ETM is defined by,

$$T(u) = E[f(t),u] = \int_0^{\infty} f(t)e^{\frac{t}{u}}\,dt, \quad u \in (-k_1, k_2) \tag{6}$$

Let *A* be an Elzaki transformable function, defined by

$$A = f(t): M, k_1, k_2 > 0, |f(t)| < Me^{|t|k_j} \text{ and}$$

$$if t(-1)^j x[0,1)\, f(t)e^{\frac{t}{u}}dt,\ u \in (k_1, k_2) \tag{7}$$

Let $T(u)$ be the Elzaki Transform of $f(t)$ or $[E(f(t)) = T(u)]$, then by integrating by parts, we obtain the following relations:

$$E[f'(t)] = \frac{T(u)}{u} - uf(0) \tag{8}$$

$$E[f''(t)] = \frac{T(u)}{u^2} - f(0) - uf'(0) \tag{9}$$

$$E[f^n(t)] = \frac{T(u)}{u^n} - \sum_{k=0}^{n-1} u^{2-n+k} f^k(0) - uf'(0);\ n \geq 1 \tag{10}$$

For details on Elzaki standard transforms of some functions, readers are referred to [11].

i. Solution of the Model using ETM

Here, we apply the Elzaki operator, E, on the model (1) – (5). For convenience, the following notations were introduced:

Let $U = q$, $I_p = w$, $I_s = x$, $V_p = y$, $V_s = z$,

$\mu_p \rho \gamma N_p = d$, $\mu_s(1-\gamma)N_s = g$ and $\mu_s \gamma N_s = c$

So that the model equation is now transformed into,

$$q'(t) = s_1 - \beta qy - \mu q \tag{11}$$

$$w'(t) = \beta qy - \alpha wz - \mu_p q \tag{12}$$

$$x'(t) = \alpha wz - \mu_s x \tag{13}$$

$$y'(t) = dw + gx - \beta qy - \delta_p y \tag{14}$$

$$z'(t) = cx - \delta dw - \delta_s z \tag{15}$$

Subject to the following initial conditions:

$q(0) = 2000,\ w(0) = 1000,\ x(0) = 100,\ y(0) = 10,\ z(0) = 10,$

and with parameter values,

$s_1 = 5,\ \mu = 0.02,\ \beta = 0.01,\ \alpha = 0.05,\ \mu_p = 0.05,\ c = 0.01$

$\mu_s = 0.05,\ \rho = 0.01,\ \gamma = 0.02,\ N_p = 10,\ N_s,\ \delta_p = 0.04,$

$\delta_s = 0.04,\ d = 0.0001$ and $g = 0.49$.

We apply the Elzaki operator, E, on (11) to obtain,

$$E[q'(t)] = E[s_1 - \beta qy - \mu q] \tag{16}$$

$$\frac{Q(u)}{u} - uq(0) = E[s_1] - \beta E[qy] - \mu E[q]$$

$$Q(u) = u^2 q(0) + uE[s_1] - \beta uE[qy] - \mu uE[q] \tag{17}$$

We now take the Elzaki inverse of (17).

$$E^{-1}[Q(u)] = q(0) - E^{-1}[s_1 u^3] - \beta E^{-1}\{uE[qy]\} - \mu E^{-1}\{uE[q]\}$$

$$q(t) = q(0) - s_1 t - \beta E^{-1}\{uE[A_{n1}]\} - \mu E^{-1}\{uE[A_{n2}]\} \tag{18}$$

where $A_{1n} = \sum_{r=0}^{n} q(r)y(n-r)$ and $A_{n2} = \sum_{r=0}^{n} q(r),\ n \geq 0$

A_{n1} and A_{n2} are the decomposers using the Adomian Decomposition Method, [12]. On substituting A_{n1} and A_{n2} into (18) and simplifying, we obtain the iterative scheme,

$$q(n+1) = q(0) - s_1 t - \beta E^{-1}\left\{uE\left[\sum_{r=0}^{n} q(r)y(n-r)\right]\right\}$$

$$- \mu E^{-1}\left\{uE\left[\sum_{r=0}^{n} q(r)\right]\right\} \tag{19}$$

Similarly, following the same procedure, we obtained the schemes for $w(n+1)$, $x(n+1)$, $y(n+1)$ and $z(n+1)$ as,

$$w(n+1) = w(0) + \beta E^{-1}\left\{uE\left[\sum_{r=0}^{n} q(r)y(n-r)\right]\right\}$$

$$- \alpha E^{-1}\left\{uE\left[\sum_{r=0}^{n} w(r)z(n-r)\right]\right\} - \mu_p E^{-1}\left\{uE\left[\sum_{r=0}^{n} w(r)\right]\right\} \tag{20}$$

$$x(n+1) = x(0) + \alpha E^{-1}\left\{uE\left[\sum_{r=0}^{n} w(r)z(n-r)\right]\right\}$$

$$- \mu_s E^{-1}\left\{uE\left[\sum_{r=0}^{n} x(r)\right]\right\} \tag{21}$$

$$y(n+1) = y(0) + dE^{-1}\left[\sum_{r=0}^{n} w(r)\right] + gE^{-1}\left[\sum_{r=0}^{n} x(r)\right]$$

$$- \beta E^{-1}\left\{uE\left[\sum_{r=0}^{n} w(r)z(n-r)\right]\right\} - \delta_p E^{-1}\left\{uE\left[\sum_{r=0}^{n} y(r)\right]\right\} \tag{22}$$

$$z(n+1) = z(0) + cE^{-1}\left\{uE\left[\sum_{r=0}^{n} x(r)\right]\right\}$$

$$- \alpha E^{-1}\left\{uE\left[\sum_{r=0}^{n} w(r)z(n-r)\right]\right\} - \delta_s E^{-1}\left\{uE\left[\sum_{r=0}^{n} z(r)\right]\right\} \tag{23}$$

Simplifying further and evaluating $n = 0, 1, 2, \ldots$, we derive the ETM iterative scheme presented as (24) – (28). This is the numerical solution of the HIV Superinfection model.

$$q(t) = 2000 - 33t - 11.14t^2 + \ldots \tag{24}$$

$$w(t) = 1000 - 33t - 11.14t^2 + \ldots \tag{25}$$

$$x(t) = 100 - 8.5t + 23.7t^2 + \ldots \tag{26}$$

$$y(t) = 10 - 3.501t + 16.57525t^2 + \ldots \tag{27}$$

$$z(t) = 10 - 11.4t + 23.632t^2 + \ldots \tag{28}$$

V. NUMERICAL SIMULATION

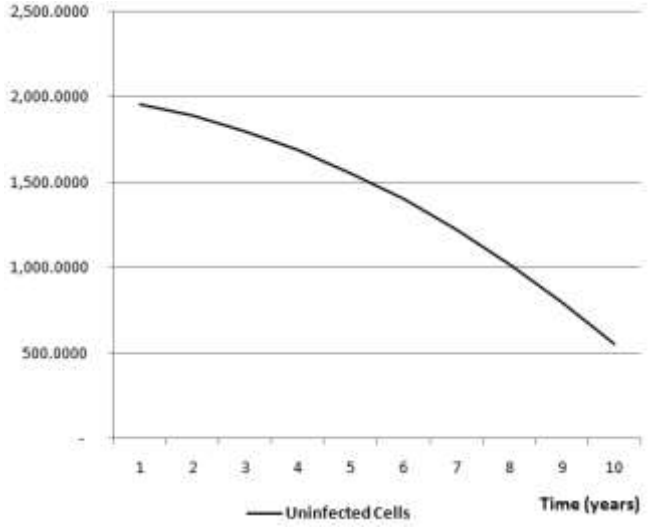

Figure 1. The plot of healthy uninfected cells versus time

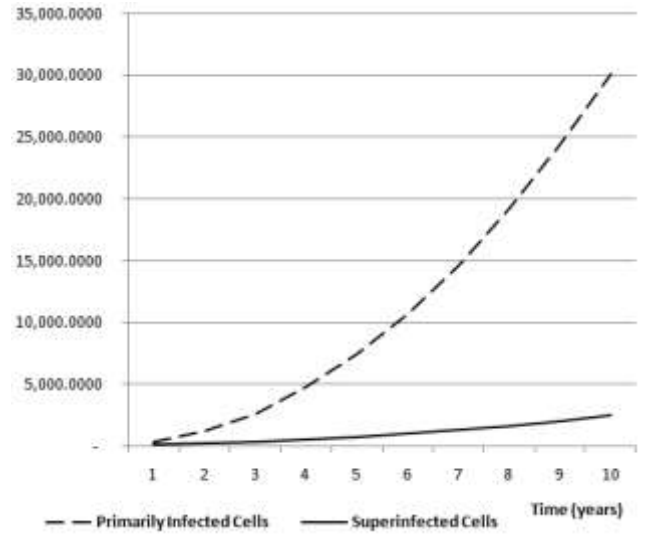

Figure 2. The plot of infected cells versus time

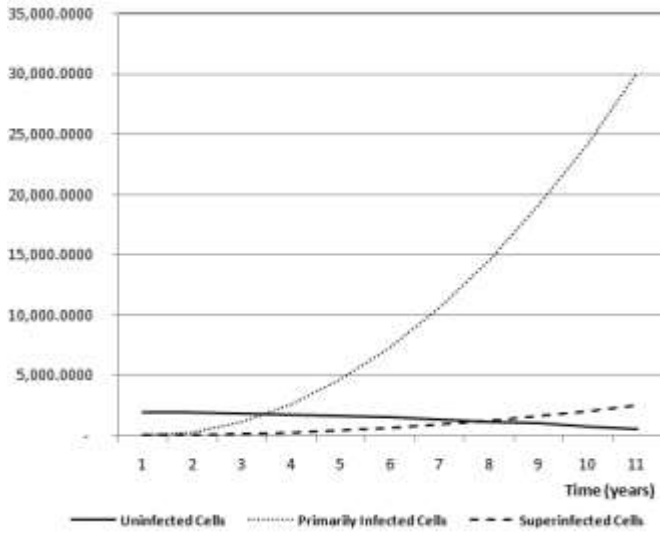

Figure 3. The plot of CD4+T cells versus time

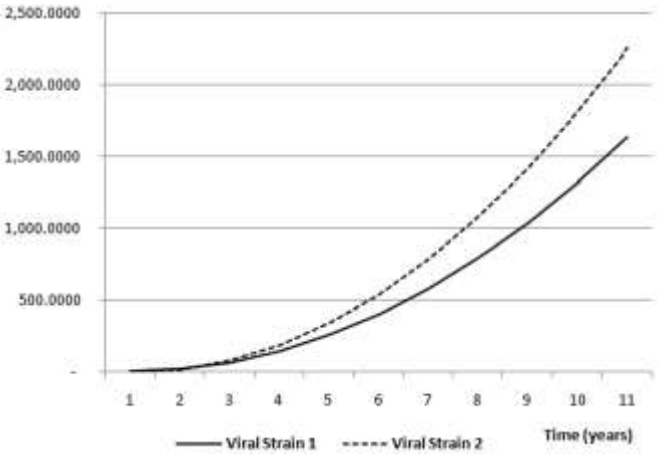

Figure 4. The plot of viral strains versus time

VI. DISCUSSION OF RESULT

The iterative scheme (24) – (28) is the solution obtained for the HIV Superinfection model using the ETM. The method provides an exact analytical solution that is known to converge faster than other traditional methods such as the Laplace Transform and Fourier Transform. It is easier to use and more efficient. This agrees with the findings of [8], [10], [11]. The scheme was used to predict the behavior of the HIV Superinfection model as seen in Fig. 1, Fig. 2, Fig. 3, and Fig. 4.

Fig. 1 shows the time plot of healthy uninfected cells. We observe a decline in the population of healthy cells. Equation (24) agrees with this. In the first iteration, $q(0) = 2000$ is obvious. Subsequently, all other terms in (24) are decreasing functions $q(t)$, so that $q(t)$ will keep declining t. The activities of viral strains are responsible for this decline. The safe level is $200mm^3$. Below this indicator, the system shall proceed from HIV to full-blown AIDS.

In Fig. 2, the graph shows the plot of primarily infected cells and superinfected cells. It can be observed that the system has been infected with two viral strains. Hence, the population of healthy cells that are observed to be declining in Fig. 1 is a result of the increase in the population of primarily infected and superinfected cells. The activities of the cells and viral strains are directly dependent.

Equations (25) and (26) represent the functions of primarily infected cells and superinfected cells respectively. In (25), only $w(0)$ is positive. All other terms are decreasing terms. But in (26), whereas the first term $x(t)$ is positive, the succeeding terms are both increasing and decreasing terms. This explains why the rate of infection of primarily infected cells is greater than that of the superinfected cells.

Fig. 3 shows the plots of uninfected cells, primarily infected cells, and superinfected cells. Whereas the populations of primarily infected and superinfected cells are on the increase, the population of uninfected cells is decreasing. The system has been engulfed and hijacked by the two viral strains. This resulted in a decline in the growth of uninfected cells. Positive growth is also observed in the population of infected cells.

Fig. 4 shows the growth of the two viral strains in the system. The two viral trains co-exist and co-circulate in the

system. It is observed that the rate of replication of V_S is slightly greater than that of V_p. (27) and (28) representing the functions for viral strain 1 and viral strain 2 respectively. By observation, all the terms in both equations are positive terms except the initial terms. The populations of the viral strains are on the increase.

VII. CONCLUSION

Several transform methods have been used in literature to solve infectious disease models. However, the Elzaki Transform Method has not been applied particularly to HIV Superinfection models. Thus, in this work, we use the Elzaki Transform Method to solve an HIV Superinfection model. The solution of the ETM gives a recursive scheme that was used to predict and interpret the behavior of the system.

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Contribution of individual authors to the creation of a scientific article (ghostwriting policy)

-Mohammed O. Ibrahim provided the basic frame work for this research.

-Matthew A. Ogunniran organized the write-up, perfomed the analysis using the ETM and was responsible for the simulation of data.

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Conflict of Interest

The authors have no conflict of interest to declare.