JEAS

JOURNAL OF ENGINEERING AND APPLIED SCIENCES

Journal of Engineering and Applied Sciences, Volume 19, Number 1, December 2021, 436-450

Genetic factor simulations for hiv infectivity in viral dynamics

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Abstract

Mathematical models of HIV/blood interactions were formulated by several researchers. Those models suffered some setbacks because they lacked actual experimental data to validate them. As a solution, values were arbitrary assigned by mathematicians and model developers to both biological processes of infectivity and control infectivity in viral dynamics. Genetic factor in HIV infectivity that assures disease progression as in reality expressed from adhesive interfacial free energy concept following the successes recorded by researchers on the role of surface thermodynamics in HIV-blood interactions is estimated from simulated infection time-course that shows a disease progression obtainable in practice. The methodology involved analytical establishment of range for genetic factors in viral dynamics since there is direct evidence of genetic factor in HIV infectivity, importing values to quantify infectivity parameter expressed through surface thermodynamics and simulating an adopted viral dynamics model incorporated with various adopted genetic factor using MATLAB^{TM} function ode 45 in ninety different simulations. The MATLAB^{TM} function ode 45 makes use of an explicit Runge-Kutta formula by numerical integration of the model. Genetic factor ε was seen to be within the range of $0 \leq \varepsilon \leq 1$. From the simulations the value of infectivity of $3 * 10^{-4}\left({}^{mL}/_{copies.d}\right)$was obtained which is within the range of infectivity values of $5.0 * 10^{-10} \leq \beta \leq 1)\left({}^{mL}/_{copies.d}\right)$arbitrarily chosen by various researchers and comparable with values that show actual disease progression. Average infectivity value obtained from the literature was used for simulation and then compared with that obtained in this study. ANOVA tests showed for uninfected cell, computed F ratio as 0.000104 which is less than the critical F ratio 4.351244, hence there was no significant difference between the average infectivity value from the literature and the HIV infectivity obtained in this study.This understanding on genetic factor in HIV infectivity would contribute potentially to stronger prevention strategies for a possible and appropriate vaccines and or more efficient drug for AIDS patients. In clinical trials and in pharmaceutical industries where drug design, drug dosing and treatment regimen depend on the infectivity, this finding will certainly be fancied.

Keywords: Adhesive Interfacial Free Energy, HIV Viral Dynamics Infectivity, Simulations, Genetic Factor

1. Introduction

There are currently twenty one families of viruses known to cause diseases in humans, including human immunodeficiency virus (HIV), Hepatitis, Herpes Simplex, Measles and they have continued to plague humans (Lai, 2014). Viruses are found in almost every ecosystem on earth and known to infect most types of organisms, including bacteria, fungi, plants, vertebrates, etc. The mechanisms by which viruses cause diseases in an organism depend largely on the viral species (Smith, 1972). Viruses can usually cause damage in the host via cell lysis, production of toxic substances and cell transformation (Doitsh & Greene, 2016). When a virus enters a cell and completes its normal replication cycle, the host cell may undergo lysis due to a physical internal pressure exerted by multiplying virus or immune response. During the course of virus replication, many cytotoxic viral components as well as by-products of viral replication accumulate in the cell (Klatt, 2015). Cell lysis and cytotoxic components cause death of the cell (Lai, 2014). If enough cells die, the whole organism will start to suffer the effects. Some viruses can cause

lifelong or chronic infections where viruses continue to replicate in the body despite the host's defence mechanisms. Ronsard *et al* cited in Santoro & Perno, (2013), noted that a rate-limiting factor in the management of HIV infections, is the plethora of genetic variations in infectivity leading to failure of clinical trials.

Variability in response to therapy has made some individuals experience virologic failure on therapy that is highly effective on others. Under the use of Highly Active Anti Retroviral Therapy (HAART), transient rebounds of plasma viremia have also remained a problem (Jeffry, 2006). Most viral diseases have the ability to develop resistance. About ten billion new viral particles of HIV can be generated daily, in chronic cases (Omenyi, 2005). Ronsard *et al* cited in (Santoro & Perno, 2013), noted that a rate-limiting factor in the management of HIV infections, is the plethora of genetic variations in infectivity leading to failure of clinical trials. Virus infectivity in HIV infection is observed to vary (Ganusov, Neher & Perelson, 2012). Clinical solution to the problem of HIV is hampered by the rapid genetic mutation of HIV. Mathematician researchers made choice of infectivity values based on the values needed to generate the dynamics of the virus and infected cells that agree with the current knowledge of HIV infection. These values were obtained either by some mere choice of values and or by using models to estimate the undefined, unexpressed interaction parameter. None of the researchers attempted to explain and give physical meaning to their *"infectivity"* parameters in viral dynamics.

This work intends to approach the problem by expressing and quantifying the "infectivity" through thermodynamic interfacial energetics and estimation of genetic factor through simulation such that there will be no arbitral choice of values for infectivity as approached by mathematician researchers. Infectivity parameter components values are imported and substituted in the proposed expression for infectivity and the value of infectivity quantified.

1.2 Literature Survey

HIV, as one of the most intensively studied viral infections, now has massive drug development efforts starting soon after identification of the virus with twenty seven (27) different antiretroviral drugs (Hill, Rosenbloom, Nowark, & Siliciano, 2018), capable of halting viral replication and preventing transmission and progression to AIDS but still without a cure. Chukwuneke, Achebe, Senibe & Ugwuegbu (2017) in one of the recent studies, observed that HIV has the tendency to reduce the interaction energy by 13% with the consequences of increased viral loads and decreased immune systems in HIV patients suffering from Tb. Achebe (2010) had earlier established a solution to HIV infection using absorbance data to derive $A_{33} \geq 0.9763 * 10^{-21}$joule as a condition for a negative A_{132} which implies net negative van dar Waals indicating repulsion between the virus and the lymphocyte. Furthermore, Ani, Omenyi & Nwigbo (2015), in their research which assert that their findings suggest a thermodynamic criterion for HIV-blood-drug interaction prediction, confirms the existence of some relationship between drug coating of surface of blood cell and the cell surface free energy by observing that the drug 1 which has highest coating effectiveness also has the highest surface free energy (47.5 MJ/m^2).

Mathematical modeling of viral dynamics, and hence HIV dynamics, provides understanding of the underlying mechanisms that influence the spread of the disease and, in the process, it suggests control strategies. The phenomenon of disease modeling can be easily accomplished through mathematical framework (Geetha, & Balamuralitharan, 2018). Since the discovery of HIV as the etiological agent of AIDS, numerous advances have been made in the understanding of the molecular biology, pathogenesis, and epidemiology of the virus, and the host immune response to it (Klatt, 2015). Not least among these has been the knowledge obtained by mathematical analysis and within-host modelling of changes in viral load and T-cell counts after initiation of potent antiretroviral therapy in individual subjects.

In the virus life cycle (replication cycle) the most crucial stage is the first stage, the binding (attachment) stage. It is a stage without which the HIV life cycle would be cut short. Now at entry to the body, the viral particle is attracted to a cell (lymphocyte) with the appropriate CD4 receptor molecules where it attaches (binds) and by fusion to a susceptible cell membrane or by endocytosis (an energy using up process) and then enters the cell. Fusion of the viral and host membranes is a critical step during infection by membrane enclosed viruses like HIV and influenza. The probability of infection is a function of both the number of infective HIV virions in the body fluid which contacts the host as well as the number of cells available at the site of contact that have appropriate CD4 receptors (Klatt, 2015: Sundquist & Kraussilich, 2012). This probability could only be attained as a result of the unavoidable contact between the virion and the lymphocyte. The interaction between a virus and the surface of the lymphocyte is controlled by a balance between electrostatic repulsion – van der Waals attraction mechanism, resulting in an adhesive energy which can be expressed as equation (1) (Omenyi, 1978).

$$\Delta F_{PLS}^{adh}(d_0) = \gamma_{PS} - \gamma_{PL} - \gamma_{SL} \quad (1)$$

Where ΔF^{adh} is the thermodynamic free energy of adhesion, integrated from infinity to the equilibrium separation distance d_o; γ_{PS} is the interfacial free energy between *P* (representing the virus) and *S* (lymphocyte), γ_{PL} is that between P and L(where *L* is the plasma) and γ_{SL} is that between S and L.

Similar equations can be obtained for interactions between the individual components as equation (2) (Omenyi, 1978).

$$\Delta F_{ij}^{adh}(d_0) = \gamma_{ij} - \gamma_{iv} - \gamma_{jv} \quad (2)$$

For all given combinations, ΔF^{adh} could be expressed in terms of van der Waals energy thereby making surface free energy or energy of interaction a function of attraction between particles suspended in a liquid medium.

1.2.1 Infectivity and Genetic Factor in HIV Infection

An approach to developing effective anti-HIV intervention is to identify and understand the molecular mechanism by which natural genetic variations provide protection from infection or disease progression. Human gene alleles that confer resistance or increased susceptibility to HIV infection are identified by this approach (Donfack, Buchinsky, Post, & Garth, 2006). Increasing data support host genetic factor as important determinants of human immunodeficiency virus type 1 (HIV-1) susceptibility (Singh & Spector, 2009). A recent evidence has indicated that natural variations in host genes can influence the outcome of HIV infection and its transmission (Lama & Planelles, 2007). Genes play a major role in determining the susceptibility or resistance to HIV-1 infection (Kumar, Prakash, Manpreet, Sumedh, & Medhi, 2006). Susceptibility to HIV infection and AIDS progression is variable among individuals and populations, and in part genetically determined (Arenzana-Seisdedos & Parmentier, 2006). There have been reports of people who were completely resistant to infection with HIV and a group of others who progressed to AIDS at a much slower rates since HIV discovery (Al-Jabri, 2007).

Anacleto *et al.* (2019) in their study in genetic differences in host infectivity, an infectivity study whose result showed that individuals can evolve different disease response types affecting epidemic survival rates, opined that there is a direct evidence for genetic variation in host infectivity. Virus infectivity in HIV infection is observed to vary (Ganusov, Neher & Perelson, 2012).

Increasing evidence however shows that risks and severity of disease depend on infectivity, which is the host ability to transmit infections. Also, in the genetic analysis of infection, host resistance to becoming infected or host ability to survive when exposed to infection is under genetic control and correlated (Anacleto *et al.* 2019).

Again, in static-dynamic infectivity relationship, it is important at this point to state as observed by Chazal, Nzounza, Pique & Ramirez (2014) in the result of their work, loss of infectivity of HIV-1 particles produced by mobile lymphocytes, that alteration of the functionality and the composition of HIV-1 particles produced by mobile lymphocyte very likely contribute to poor efficiency of HIV-1 replication in shaken T-cell cultures. Their result showed a tenth of infectivity of mobile lymphocytes when compared with the static ones. They showed that infectivity rate at static condition is about 10 times the ideal situation, where blood in the circulatory system is in constant motion (shaking). The relationship between infectivity at static and mobile condition of lymphocyte is such that infectivity at mobile condition is one-tenth of that at static condition.

$$Infectivity_M = \psi Infectivity_S \quad (3)$$

Where $Infectivity_M$ is infectivity under ideal condition, that is when the blood is mobile resulting to mobile lymphocyte and $Infectivity_S$ is infectivity under static condition when the blood is static and not circulating. Worthy of note is that effect of genetic variation in host infectivity (genetic variance) is already felt in the infectivity under static condition, that is $Infectivity_S$ is a function of genetic variation.

1.2.2 Basic Viral Dynamics

In the solution of HIV viral dynamics (a field of applied mathematics) which is a set of complex nonlinear differential equations (see eq. 4) that describe changes over time in the populations of cells targeted by the virus and viral load, numerical technique is resorted to, due to challenges of lack of analytical technique on non-linear differential equation since numerical technique provides approximate solutions.Magnitude of data involved also posed a challenge.

The healthy cells are infected by the virus at a rate that is proportional to the product of their population size and the amount of free virus particles with a constant that is an indication of the effectiveness of the infection process (Bonhoeffer, May, Shaw, and Nowak, 1997; Hill, Rosenbloom, Nowark, & Siliciano,2018). It is known that from pathogenesis of HIV infection that retroviruses are unable to replicate outside of living host cells and do not contain deoxyribonucleic acid (DNA). The pathogenesis of HIV infection is a function of the virus life cycle, host cellular environment, and quantity of viruses in the infected individual. In the virus life cycle (replication cycle) the most crucial stage is the first stage, the binding (attachment) stage. It is a stage without which the HIV life cycle would be cut short. Now at entry to the body, the viral particle is attracted to a cell (lymphocyte) with the appropriate CD4 receptor molecules where it attaches (binds) and by fusion to a susceptible cell membrane or by endocytosis (an energy using up process) and then enters the cell. These reasonings enabled researchers, notably Bonhoeffer, *et al.*, (1997), to propose a basic model of viral dynamics as:

$$\begin{aligned} \dot{x} &= \lambda - dx - \beta xv, \\ \dot{y} &= \beta xv - ay, \\ \dot{v} &= ky - uv. \end{aligned} \qquad (4)$$

Where x is susceptible cells, y is infected cells, v is virus particle, λ is rate of production of susceptible cells, d is death rate of susceptible cells, β is infectivity (interaction parameter), a is death rate of infected cells, k is rate of virus production and u is clearance rate of virus particles.

The true infection time course situations are presented in figures 1a to 1d for time course of uninfected cells in a typical infection progression obtainable in a typical uncontrolled infection. In each of the plots, there is an initial wave-like oscillation in few days to about six weeks with not less than five hundred cells per μL, 500 $\left({}^{cells}/_{\mu L}\right)$ which later experience some dampening effects by converging to equilibrium which is within the range of $CD4^+$ T cell count between two hundred and four hundred and ninety-nine (200-499) cells per μL (mm^{-3}) representing the stage two known as the asymptomatic or clinical latency or chronic infection stage.

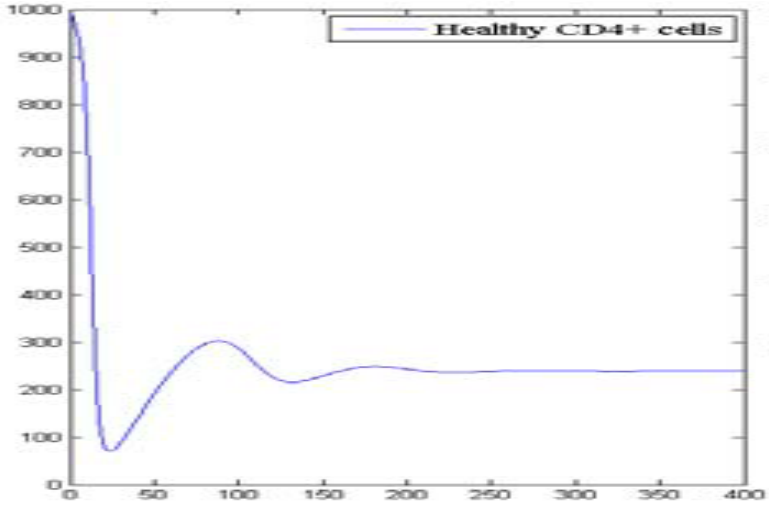


Figure 1a:Uninfected cell in $\left({}^{cells}/_{\mu L}\right)$ time-course (Moyosis & Kafetzis, 2016)

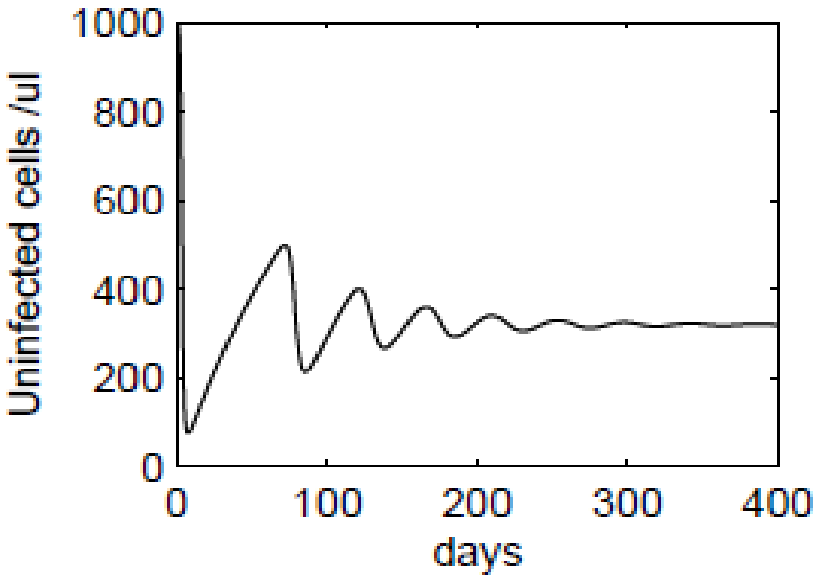


Figure 1b:Uninfected cell time-course(Wang & Zhou, 2010)

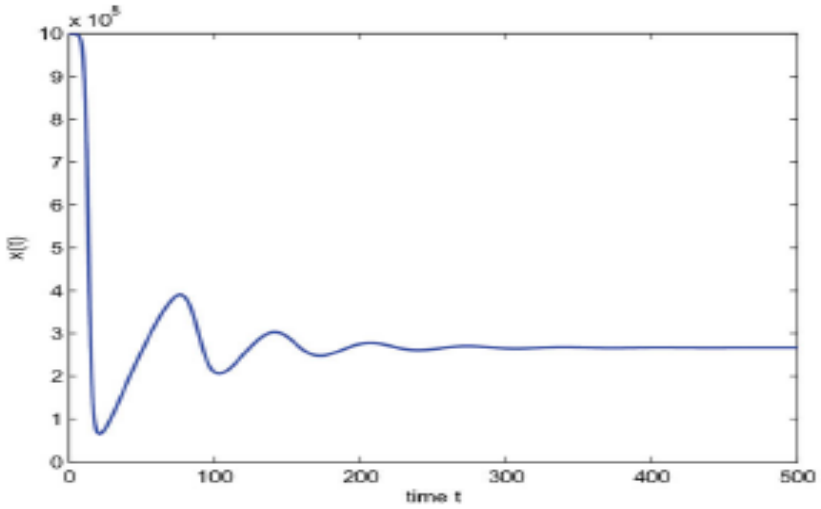


Figure 1c:Uninfected cell in $\left({}^{cells}/_{mL}\right)$time-course(Xu, Tian & Zhang, 2018)

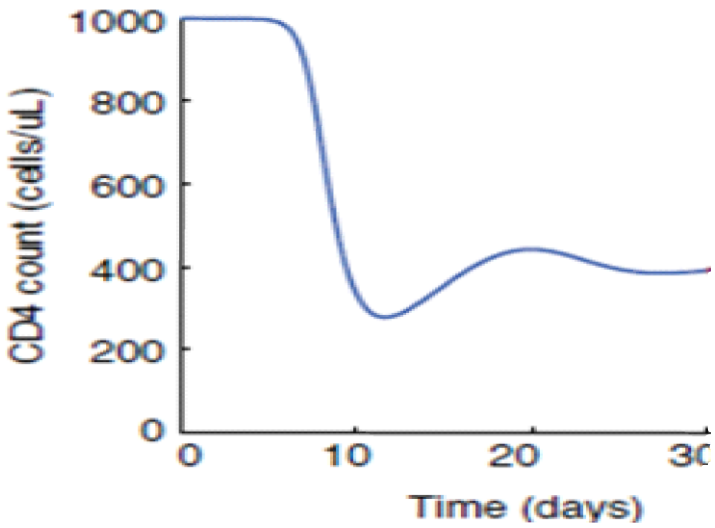


Figure 1d: Uninfected cell time-course for thirty days (Hill et al, 2018)

Figures 1a to 1d show normal disease progression in reality from zero day of infection period. The figures are what the expected simulation result is expected to look like. Little or no effort has been put into the understanding of the promoters of the virus binding effects on the lymphocytes in the studies on mathematical modelling as reported so far. In this paper therefore, the virus/blood interaction parameter required for complete solution of the model equations, will be expressed using interfacial energetics concepts and simulations made to estimate the infectivity parameter.

1.3 Scope and Justification of the Work Done

In this work, only HIV/human blood interactions is considered with the use of van der Waals forces as analytical tool, in the absence of antiretroviral drugs environment. Data is imported from available literature to quantify surface energetics and interfacial free energy. Existing basic viral dynamics models is adopted for the study. The mathematical models will be solved using MATLAB FUNCTION ODE 45 solution tools. Time dependent interaction parameter, genetic variation factor and mutation problems shall not be sought for in this study as genetic variation factor is estimated. Surface thermodynamics of the antiretroviral drugs used in HIV treatment is definitely beyond the scope of this work. Those in the pharmaceutical industry who are involved in antiretroviral drug design and production will value this work. The success of the research, when it leads to appropriate drug design and production, based on appropriate information of surface thermodynamics of HIV infectivity will be of benefit to pharmaceutical industries, clinicians and HIV/AIDS patients.

2.0 Material and methods

2.1 Material and data

The data used to study the models of interaction include those of the Antiretroviral drugs as quantified by (Ilo, 2021). Equipment include a HP laptop model HP 620 while software is a computerized program for solving sets of complex nonlinear differential equations that makes use of explicit Runge-Kutta formula in MATLAB^{TM} function ode 45 in numerical integration of the model.

2.2 Model Solution Procedure

The methodology involved expressing infectivity in viral dynamics through surface thermodynamics, importing data for adhesion driven parameter from (Ilo, 2021), analytical establishment of range for genetic factors in viral dynamics since there is direct evidence of genetic factor in HIV infectivity, and simulating an adopted viral dynamics model (eqn 4) incorporated with various adopted genetic factorusing MATLAB^{TM} function ode 45 in ninety different numerical simulations for a progression or infection time course as in reality. The MATLAB^{TM} function ode 45 makes use of an explicit Runge-Kutta formula by numerical integration of the model. The infectivity value is obtained from the numerical simulation plot with progression as in reality and the expression for infectivity equation (5).

2.3 Infectivity (Virus Mechanism of Action) Expressed as Adhesion Coefficient β_{0T}

From literature, HIV infection is a function of genetic factor and the infection driving factor (adhesion driven parameter) and that since data for infectivity parameter was taken at static condition, the static to dynamic conversion factor of equation (3) was introduced. Thus expressed infectivity is as shown in equation (5),

$$\beta_{0T} = \varepsilon\left(\frac{\psi(\gamma_{PS})}{\gamma_{PL}+\gamma_{SL}}\right)(0 < \beta_{0T} \leq 1) \qquad (5)$$

Equation (5) shows a direct evidence of genetic factor ε in infectivity and direct variation with the infection adhesion driven parameter $\gamma_{PS}/_{(\gamma_{PL}+\gamma_{SL})}$ from equation (1), bearing in mind that in the HIV particle/blood cell interaction, infectivity is adhesion driven, and so the infectivity which invariably is a function of efficiency of the adhesion has a maximum value of one (1) and is therefore termed adhesion coefficient with notation $\beta_{0T}$with the unit of$\left(mL/_{copies.d}\right)$.

2.4 Genetic Factor Range

From literature review, it is evident that genetic factor provides either resistance or susceptibility to HIV infection. In other words, protection from HIV infection which is resistance or disease progression which is susceptibility to disease is enabled or assured by genetic factor. This genetic factor according to Ilo (2021) is denoted with the symbol ε. As observed by (Anacleto *et al.* 2019) that there is direct evidence of genetic factor in HIV infectivity, in principle it would mean that at complete resistance to HIV infection, the genetic factor ε has a value of zero (0), on the other hand, when the resistance by the genetic factor is completely lost for disease progression that is susceptibility, then in principle, the genetic factor ε allows the disease to progress hundred per cent (100%) according to infectivity parameter, hence the genetic factor has a value of one (1), meaning complete susceptibility.

Table 1 gives values for components of infectivity, expectedgenetic factor range and adhesion driven parameter utilised in numerical simulation. The unit of γ_{PS} is $\left(mL/_{copies.d}\right).\left(mJ/_{m^2}\right)$, for γ_{PL} and γ_{SL} is $\left(mJ/_{m^2}\right)$, and adhesion driven parameter unit is $\left(mL/_{copies.d}\right)$.

Table 1:Computed infectivity parameter components (Ilo, 2021)

γ_{PS} $\left(mL/_{copies.d}\right)\left(mJ/_{m^2}\right)$	γ_{PL} $\left(mJ/_{m^2}\right)$	γ_{SL} $\left(mJ/_{m^2}\right)$	Genetic factor range, ε -	Adhesion driven parameter $\left(mL/_{copies.d}\right)$
39.10	19.87	19.67	0-1	$1*10^{-1}$

To determine genetic factor that assures a disease progression that is real, ninety different simulations were made with a set of adopted viral dynamics complementary parameters from the literature and ninety different genetic factor values in conjunction with equation (5). For reference purposes, the ninety different simulations are reported and could be accessed in (Ilo, 2021).

3.0 Results and Discussions

3.1 Results of Infection Time-Course from Numerical Simulations of Viral Dynamics

Sample for the population of the ninety simulations results are shown in figure 2, 3, 4, 5 and 6. In the interpretation of figure 2, one could see a disease progression that is far from what obtains in reality. It is not comparable to the findings and simulation progression of Moyosis & Kafetzis (2016), Wang & Zhou (2010), Xu, Tian & Zhang (2018) and Bill *et al.*, (2018) which are all shown in the referenced plots of figures 1a to 1d. Here, the system converges to equilibrium with infected cells and infective virus particles. In less than a day, there is a very sharp rise in both the

number of infected cells and virus particles which causes a corresponding sharp decrease in the number of susceptible cells. After this the infected cells and virus particles decline and then tend to their equilibrium values. This equilibrium is reached very quickly in just about six days where uninfected cells dropped to about 0 cells per μL, 0 $\left({cells}/{\square L}\right)$in less than a quarter of a day. Figures 3 to 5 do not follow the same trend as in figure 1 as explained earlier. Therefore, figures 3 to 5 are not comparable to the findings and simulation progression of Moyosis & Kafetzis (2016), Wang & Zhou (2010), Xu, Tian & Zhang (2018) and Bill *et al.*, (2018) which are all shown in the referenced plots of figures 1a to 1d. In the next, figure 3, uninfected cells dropped to about 0cells per μL, 0 $\left({cells}/{\square L}\right)$in about a quarter of a day. In figure 4, uninfected cells first dropped to about 0 cells per μL, 0 $\left({cells}/{\square L}\right)$in less than three days. In figure 5,uninfected cells dropped to about 0 cells per μL, 0 $\left({cells}/{\square L}\right)$in about one and half days. All these, figures 3 to 5 are therefore not accepted for estimation of infectivity value because they do not follow the trend of figures 1a to 1d hence are not comparable to the findings and simulation progression of Moyosis & Kafetzis (2016), Wang & Zhou (2010), Xu, Tian & Zhang (2018) and Bill *et al.*, (2018) which are all shown in the referenced plots of figures 1a to 1d. All the simulations for estimation of genetic factor are reported by Ilo, (2021).

In contrast to progression, figure 6 is a replica of figures 1a to 1d which shows simulated time-course of uninfected cells in a typical infection progression obtainable in a typical uncontrolled infection. In figure 6, there is an expected initial wave-like oscillation of uninfected cells which later experience some dampening effects by converging to equilibrium which is within the range of $CD4^+$ T cell count which occurs from two hundred to four hundred and ninety-nine, i.e., from 200-499$\left({cells}/{\square L}\right)$. This represents the stage two known as the asymptomatic or clinical latency or chronic infection stage. The simulation results of figure 6 are comparable to the findings and simulation progression of Moyosis & Kafetzis (2016), Wang & Zhou (2010), Xu, Tian & Zhang (2018) and Bill *et al.*, (2018) which are all shown in the referenced plots of figures 1a to 1d.

Discussions above from results of the ninety different numerical simulations show that figure (6) established disease progression that is obtainable in reality, hence the infectivity value of $3 * 10^{-4}\left({mL}/{copies.d}\right)$is obtained and accepted for this study using equation (5). Again, the obtained infectivity value is also within the established range $(0 < \beta_{0T} \leq 1)\left({mL}/{copies.d}\right)$as seen in Ilo (2021) and $(5.0 * 10^{-10} \leq \beta \leq 1)\left({mL}/{copies.d}\right)$chosen or assigned by various researchers.

Figure 2, 3, 4, 5 and 6 are shown below.

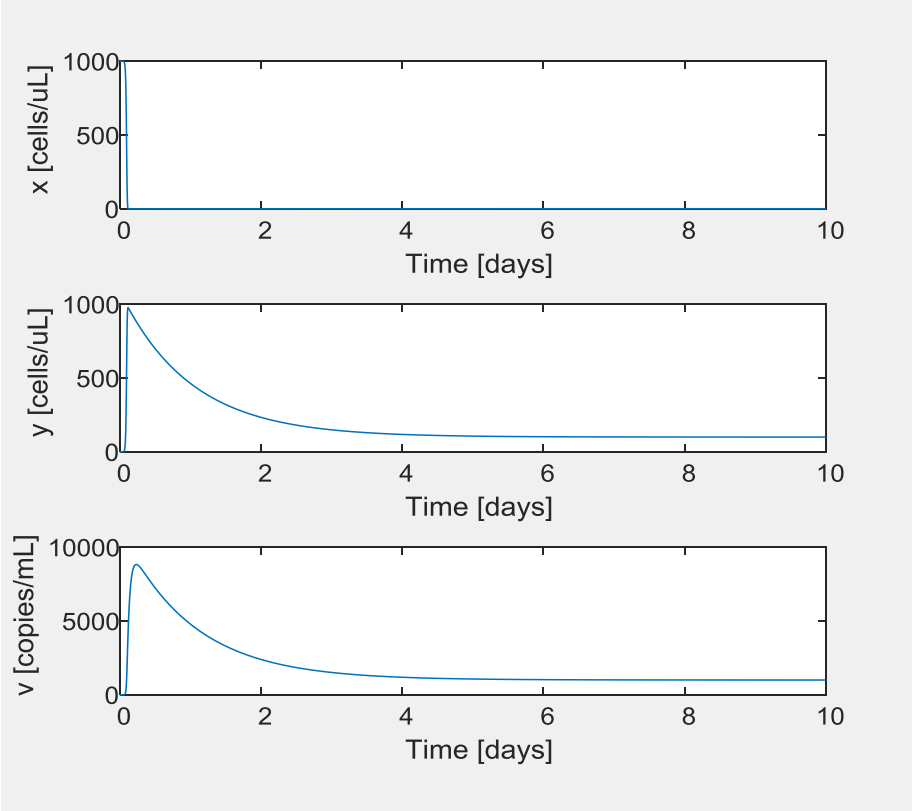


Figure 2: Trial simulation with genetic factor value of 1 for infectivity of $1 * 10^{-1}$ $\left({}^{mL}/_{copies.d}\right)$.

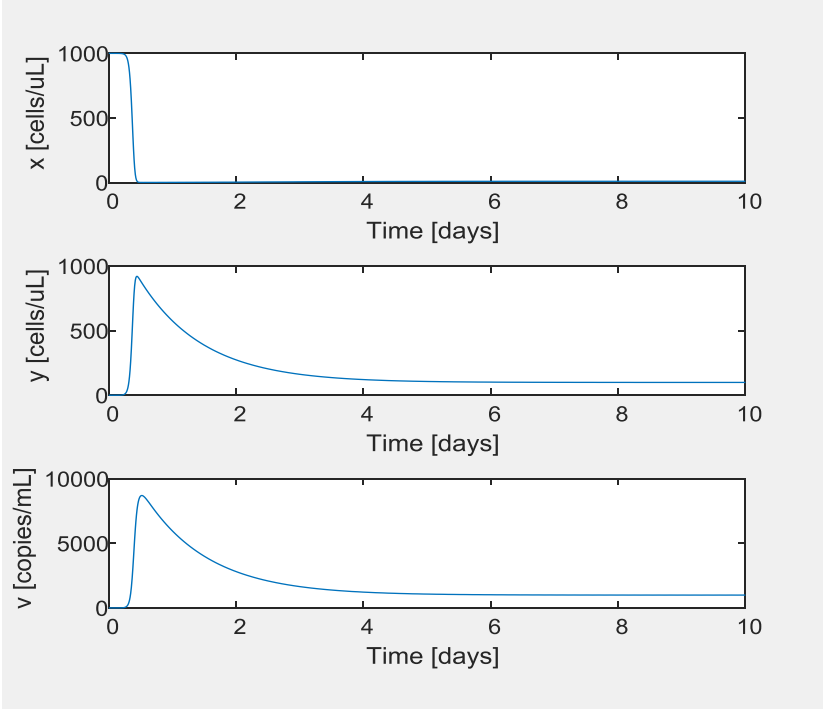


Figure 3: Trial simulation with genetic factor value of 0.1 for infectivity of $1 * 10^{-2}$ $\left({}^{mL}/_{copies.d}\right)$.

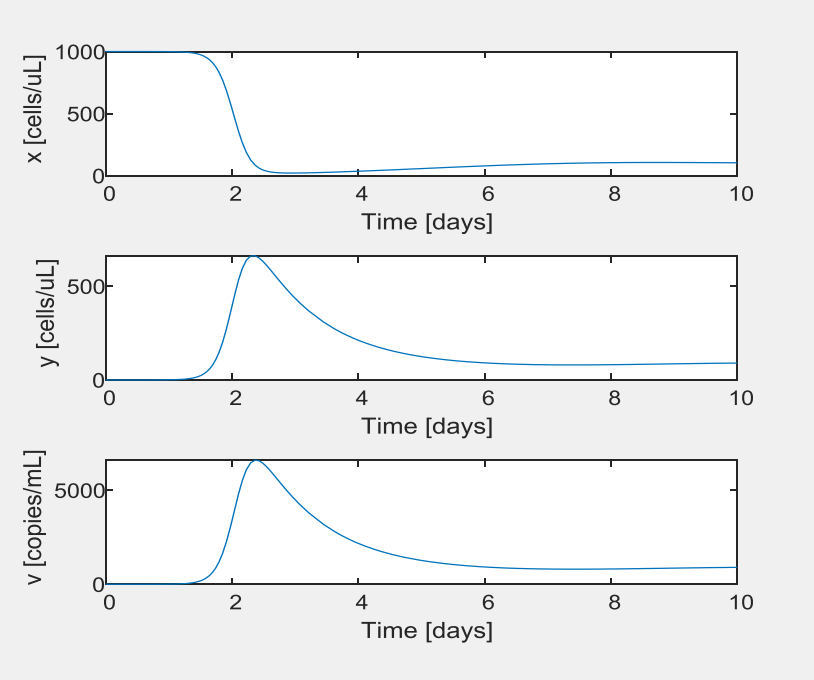


Figure 4: Trial simulation with genetic factor value of 0.01 for infectivity of $1 * 10^{-3}$ $\left(mL/_{copies.d}\right)$.

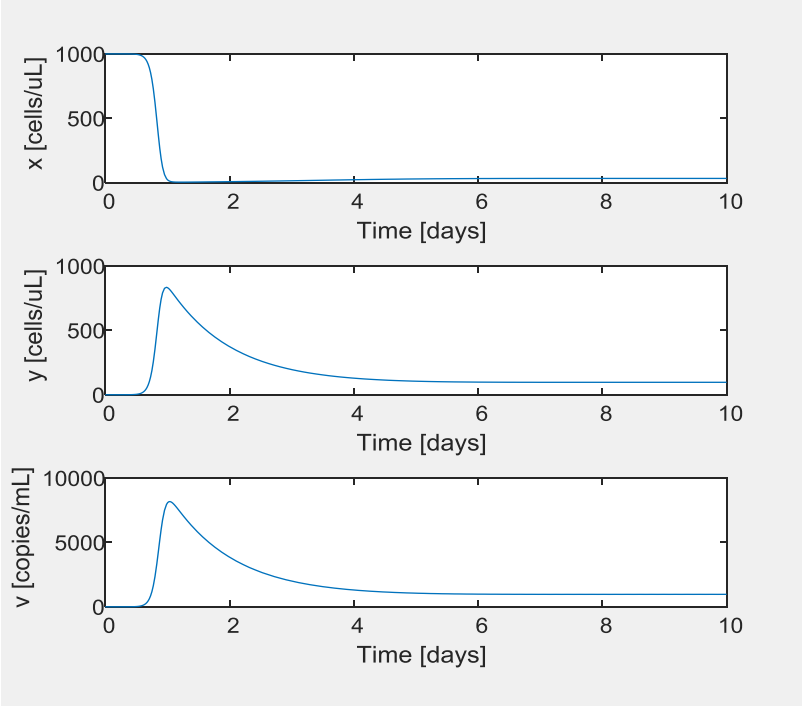


Figure 5: Trial simulation with genetic factor value of 0.03 forinfectivity of$3 * 10^{-3}$ $\left(mL/_{copies.d}\right)$.

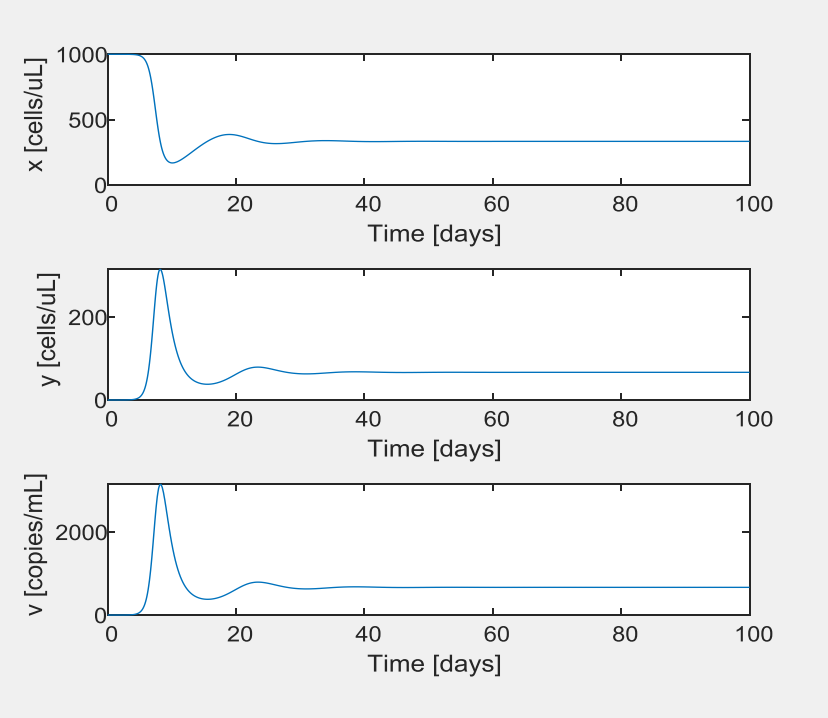


Figure 6: Trial simulation with genetic factor value of 0.003 forinfectivity of $3 * 10^{-4}\left(mL/_{copies.d}\right)$.

Figures 1a to 1d show disease progression with varied genetic factor hence the infectivity. The effect of genetic factor in each figure is clearly evident.

3.2 Validation of Results

This work involved the determination of HIV infectivity in viral dynamics by simulations for genetic factor using the viral model equation and comparing the same with HIV infectivity in viral dynamics reported in the literature. For validation purposes, numerical simulations with genetic factor characterized infectivity values obtained in this work were plotted alongside those from average infectivity values obtained from the literature Ilo(2021) and are shown in figures 7 and 8 for uninfected and infected cells respectively. Series A represent genetic factor characterized infectivity obtained in this study while series B is one with literature average infectivity value.

For Uninfected cells:

In figure 7, the progression of uninfected cell time-course of series A and series B shows a coincidence for the two series. This coincidence is an indication that the uninfected cell time-courses resulting from simulation of the adopted viral dynamics with genetic factor characterized infectivityand reviewed infectivity averagecorrespond essentially in all aspects.

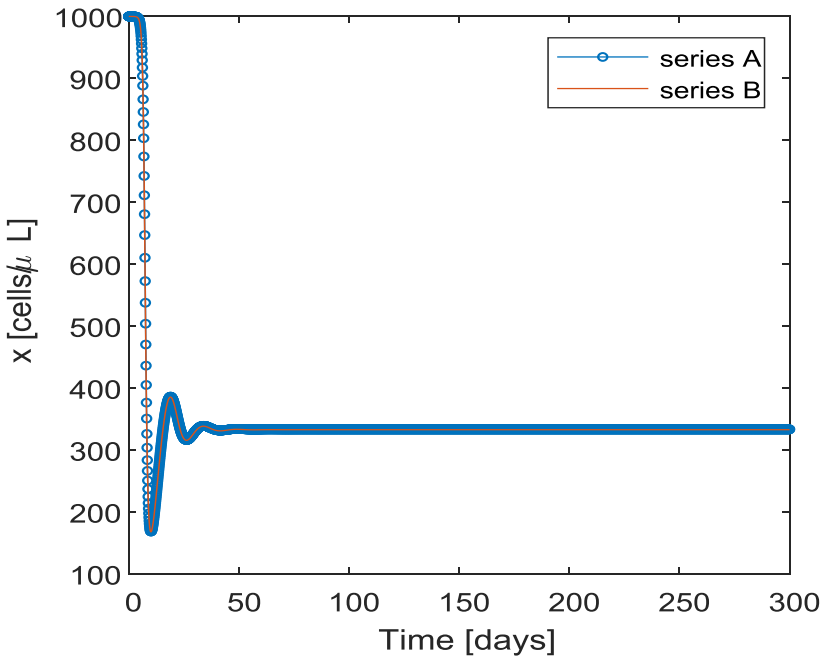


Figure 7: Comparative plots of uninfected cell time-course with genetic factor characterized infectivity, series A and that with average literature infectivity value, series B.

Figure 7: shows uninfected cell time-course of uncontrolled Infectiondynamics of series A alongside uninfected cell time-course of uncontrolled Infection dynamics of being series B both for 300 and 50 days. Common parameters are$\lambda = 100(cells/\mu L/d)$, $k = 250(copies/cell/d)$, $d = 0.1(d^{-1})$, $a = 1(d^{-1})$, $u = 25(d^{-1})$, $x_{(0)} = {\lambda}/{d}\,(cells\mu L^{-1})$, $y_{(0)} = 10^{-3}(cells\mu L^{-1})$ and $v_{(0)} = 0(copiesmL^{-1})$. Uncommon parameters are,$\left(\frac{\psi(\gamma_{PS})}{\gamma_{PL}+\gamma_{SL}}\right) = 0.1\left({mL}/{copies.d}\right)$, $\beta = 3.00539 * 10^{-4}\left({mL}/{copies.d}\right)$.

For Infected cells

In figure 8, the progression of infected cell time-course of series A and series B shows a coincidence for the two series. This coincidence is an indication that the infected cell time-courses resulting from simulation of the adopted viral dynamics with both genetic factor characterized infectivity and reviewed infectivity average correspond in essential respect.

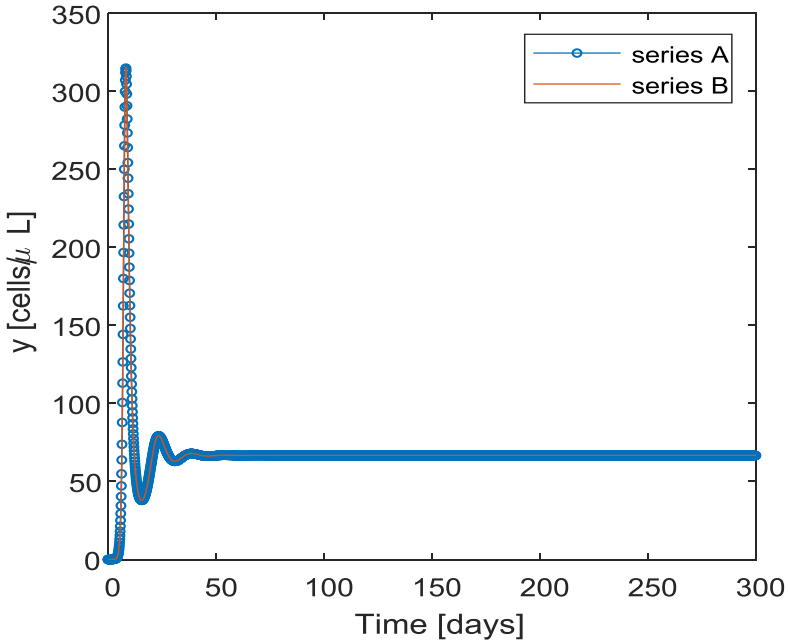


Figure 8: Comparative plots of infected cell time-course with genetic factor characterized infectivity, series A and that average literature infectivity value, series B.

Figure 8 shows infected cell time-course of uncontrolled Infection dynamics of series A alongside infected cell time-course of uncontrolled Infection dynamics of series B both for 300 and 50 days. Common parameters are $\lambda = 100(cells/\mu L/d)$, $k = 250(copies/cell/d)$, $d = 0.1(d^{-1})$, $a = 1(d^{-1})$, $u = 25(d^{-1})$, $x_{(0)} = {}^{\lambda}/_{d}\,(cells\mu L^{-1})$, $y_{(0)} = 10^{-3}(cells\mu L^{-1})$ and $v_{(0)} = 0(copiesmL^{-1})$. Uncommon parameters are, $\left(\frac{\psi(\gamma_{PS})}{\gamma_{PL}+\gamma_{SL}}\right) = 0.1\left({}^{mL}/_{copies.d}\right)$, $\beta = 3.00539 * 10^{-4}\left({}^{mL}/_{copies.d}\right)$. The data used to plot figures 7 and 8 were also subjected to ANOVA tests and it was found that in the twocases, there was no significant difference between these data.

4.0. Conclusion

Explanations to the plethora of genetic variations in infectivity leading to failure of clinical trials has been traced to wide range of genetic factor values and adhesion driven parameter in HIV infectivity hence plethora of HIV disease progression. Concluding this work therefore, an option of preventing or counteracting HIV-blood interaction could be achieved by actually quantifying adhesion driven parameter and the genetic factor in HIV infectivity hence the infectivity. Infectivity value of $3 * 10^{-4}\left({}^{mL}/_{copies.d}\right)$was obtained which is within the range of infectivity values $(5.0 * 10^{-10} \leq \beta \leq 1)\left({}^{mL}/_{copies.d}\right)$chosen or assigned by various researchers. Comparative plots of simulation results with reviewed average infectivity show that the simulation with estimated genetic factor gave an infectivity that gave a disease progression that is obtainable as in reality. Attention in future should be geared towards use of this approach to determine the infectivity hence the disease state of patients for appropriate drug regimen. Issues concerning time dependent interaction parameter and genetic factor in HIV infection expression will be sought for in future.

5.0 Recommendation

Quantification of infectivity through surface thermodynamics (adhesion driven parameter) and genetic factor in HIV infectivity is also a novel one. This understanding on adhesion driven parameter and genetic factor resistance against HIV would contribute potentially to stronger prevention strategies for a possible and appropriate vaccines and or

more efficient drug for AIDS patients. This will lead to an effective control mechanism approach. The application of this study in pharmaceutical industries, in the area of drug design and in clinical studies cannot be overemphasized. The findings of this work could be used in any other approach used to define or express HIV infectivity where adhesion driven parameter and genetic factor are needed to quantify infectivity especially in clinical trials and in pharmaceutical industries where drug design, drug dosing and treatment regimen depend on the infectivity. Drug dosing should rely much on the result of this research. Clinicians should explore the potentials of these findings.

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