ISSN 2393-8471

International Journal of Recent Research in Civil and Mechanical Engineering (IJRRCME)
Vol. 11, Issue 1, pp: (61-66), Month: April 2024 – September 2024, Available at: www.paperpublications.org

THERMODYNAMICS EXPLANATION OF PLETHORIA OF INFECTIVITY IN HIV DYNAMICS

Ilo, C. P. [1*], Omenyi, S. N. [2], Dim, E. C. [1]

[1] Department of Mechanical and Production Engineering, Enugu State University of Science and Technology, Enugu, Nigeria.

[2] Department of Mechanical Engineering, Nnamdi Azikiwe University, P.M.B 5025, Awka, Anambra State, Nigeria

DOI: https://doi.org/10.5281/zenodo.13853760

Published Date: 28-September-2024

Abstract: **Thermodynamic expressed infectivity model is incorporated in an adopted basic viral dynamics model and the ensued model solved simultaneously with five different genetic factors, $\varepsilon = 0$; $\varepsilon = 2.0 \text{ x } 10^{-3}$; $\varepsilon = 3.0 \text{ x } 10^{-3}$; $\varepsilon = 6.0 \text{ x } 10^{-3}$ and $\varepsilon = 7.0 \text{ x } 10^{-3}$ that are within genetic factor range for a five series plot of mauve, black, green, blue and red respectively to x-ray implications of genetic factor in the dynamics of HIV infection. Historical data that were used to quantify the expressed model were that of historical interfacial free energetics. The adopted basic viral dynamics model is an Ordinary Differential Equation (ODE). The solution of the ensued model from numerical integration that utilized explicit Runge-Kutta method is simulated for the infection time course using MATLAB^{TM} function ode 23. The infection dynamics was allowed to progress from day zero to about 300 day for the first instance to x-ray the dynamics up to equilibrium point and at the second instance to x-ray the initial oscillatory dynamics which is an acute consequence of genetic factor. The solution showed dynamics as expected. Comparatively and for validation of the model in principle, the black series with $\varepsilon = 2.0 \text{ x } 10^{-3}$, the best genetic factor of all the infective series produced infection time course with the highest CD4$^+$ T cell count of about (350-499) cells per µL ($cells\mu L^{-1}$) as compared to the red series with $\varepsilon = 7.0 \text{ x } 10^{-3}$, the worst genetic factor that produced infection time course with lowest CD4$^+$ T cell count of about (250-350) cells per µL ($cells\mu L^{-1}$). This goes a long to unravel the plethoria of infectivity in HIV dynamics. Comprehensively, uninfected cell CD4$^+$ T cell count is seen to be between two hundred and four hundred and ninety-nine (250-499) cells per µL ($cells\mu L^{-1}$) which is line with the literature which says that within the first eight years, uninfected cell CD4$^+$ T cell count is between two hundred and four hundred and ninety-nine (200-499) cells per µL ($cells\mu L^{-1}$). The oscillatory dynamics is as a result of initial vigor by the genetic factor trying to battle down the infection while the infection driving parameter tries to resist the action of the genetic factor hence the oscillation. What a thermodynamic onslaught and counter onslaught. One thing is worthy of note, and that is the fact that the genetic factor zero that gave infectivity value of 0$\left({}^{mL}/_{copies.d}\right)$ was able to resist the infection as seen in series with mauve colour with the uninfected cell count maintained a constant value 1000 cells per µL ($cells\mu L^{-1}$) while in other values of genetic factors that made the infected cells susceptible, the infection progressed as expected. The result of this paper explains the fact that there is plethoria of infectivity in HIV dynamics hence the need for a therapeutic approach that takes cognizance of individual genetic factor, as genetic factor characterization forms the front of future studies. The application of this study in pharmaceutical industries, in the area of drug design and in clinical studies cannot be overemphasized.**

Keywords: **Human immunodeficiency virus, Interfacial energetics, Infectivity, Genetics.**

ISSN 2393-8471

International Journal of Recent Research in Civil and Mechanical Engineering (IJRRCME)
Vol. 11, Issue 1, pp: (61-66), Month: April 2024 – September 2024, Available at: www.paperpublications.org

1. INTRODUCTION

Virus infectivity in HIV infection is observed to vary (Ganusov, Neher & Perelson, 2012). Ronsard *et al.*, 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. 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. 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). Clinical solution to the problem of HIV is hampered by the rapid genetic mutation of HIV.

Life at the molecular level is instructed to grow and reproduce while in organisms, thermodynamic governed FGI controls gene expression, thus maintaining the low entropy, homeostatic state necessary for organisms to survive and reproduce. All known life forms depend on having the correct FGIs maintained in their cells. All cells and subsequent species construction, were governed by the most fundamental of all laws—the laws of thermodynamics (Trevors and Saier, 2011). Living organisms are programmed by functional genetic instructions (FGIs), which flow through a biochemical communication pathway involving DNA –RNA- proteins, to instruct cells how to assemble into living organisms achieved by absorption of energy.

Actual mechanisms of virus/blood interactions parameters identification, within the existing mathematical models has not been easy. Unavailability of experimental data on HIV/blood interactions remained very serious problem in the mathematical modelling. The impetus to unravel interfacial energetics and genetics in HIV discordant couples is rooted on the following successes in HIV through thermodynamics. Ilo, Omenyi, and Dim, (2021a) had applied thermodynamics in the dynamics of HIV. Ilo, Omenyi and Ani, (2021b) had quantified drug primary mechanism of action through thermodynamics Hamaker concept. Ilo, (2022) through thermodynamics spectrophotometry gave an insight control infectivity in HIV dynamics. Ilo, (2024a) had developed a validated model through concepts of thermodynamics implementation to unravel the mystery of transcriptional bifurcation in HIV dynamics. Ilo, (2024b) had also established HIV adhesion driven infectivity through electrostatics interaction mechanism. In this paper, genetic factor in infectivity explains thermodynamically the plethoria of infectivity experienced in HIV infections.

2. PREVIOUS WORK/LITERATURE SURVEY

Viral Dynamics

Numerical technique is resorted to, due to challenges of lack of analytical technique on non-linear differential equation since numerical technique provides approximate solutions of HIV viral dynamics model (a field of applied mathematics) which is a set of complex nonlinear differential equations (1) that describe changes over time in the populations of cells targeted by the virus and viral load. Magnitude of data involved also posed a challenge.

The pathogenesis of HIV infection is a function of the virus life cycle, host cellular environment, and quantity of viruses in the infected individual. It is also 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 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). A stage without which the HIV life cycle would be cut short in the virus life cycle (replication cycle) is the first stage, the binding (attachment) stage. 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 during entry to the body. These reasonings enabled researchers, notably Bonhoeffer, *et al.*, (1997), to propose a basic model of viral dynamics as:

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

ISSN 2393-8471

International Journal of Recent Research in Civil and Mechanical Engineering (IJRRCME)
Vol. 11, Issue 1, pp: (61-66), Month: April 2024 – September 2024, Available at: www.paperpublications.org

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.

Three (3) main stages, namely the acute HIV infection (primary infection), asymptomatic and the advanced – aids as clearly shown in a typical HIV infection course Fig. 1 have been identified in HIV infection dynamics. Antibodies to the virus may develop in about a week to several months or more after infection with HIV and one could test positive on antibody test after antibodies to HIV appear in the blood as depicted in Fig. 1.

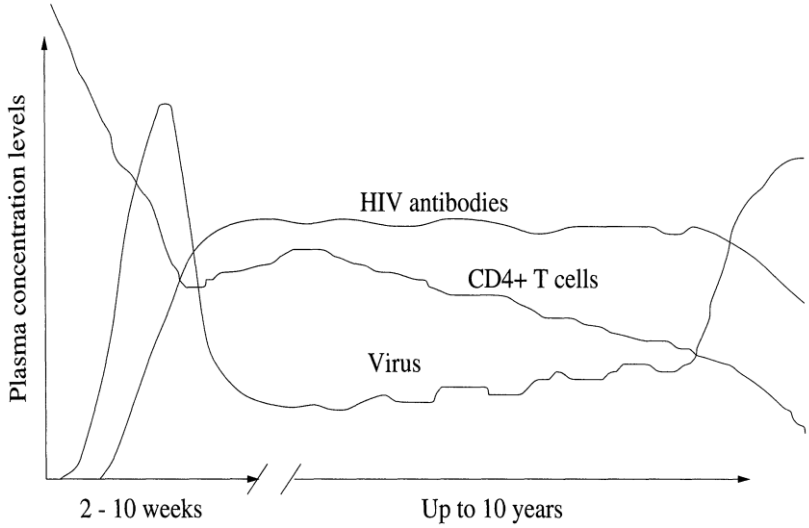

Figure 1: Approximate Time-Course of HIV Infection, (Witten and Perelson, 2004; Perelson and Nelson, 1999).

When infection is not yet established, normal $CD4^+$ T cell counts range from five hundred (500) to one thousand six hundred (1600) cells per cubic micro litre, on the average (1000) cells per cubic micro litre and drops to less than hundred (500) cells per µL (cells mm^{-3}) if infection is fully established.

Asymptomatic Stage of infection:

As the name implies this means without symptoms. This period of infection is also known as the clinical latency period. One with HIV infection does not exhibit any evidence of disease or any clinically noticeable ill effects, even though HIV is continuously infecting new cells and actively replicating. During the asymptomatic period, HIV is active within lymphoid organs where large amounts of virus become trapped in the follicular dendritic cell network, (ATIS, 2002). At this stage, the $CD4^+$ T cell count is between two hundred and four hundred and ninety-nine (200-499) cells per µL ($cells\mu L^{-1}$) about 14%-28% of all lymphocytes and the stage can last for eight (8) years or more (Nettleman and David, 2021). The normal duration of untreated individuals ranges from seven to ten years. Nevertheless, this period of clinical latency has a wide variation in length from one person to another. There are reports of this latency period lasting for more than 15 years and some lasting just two years, (Jeffry, 2006).

Genetic Factor Range

Protection from HIV infection which is resistance or disease progression which is susceptibility to disease is assured or permitted by genetic factor. It is evident that genetic factor provides either resistance or susceptibility to HIV infection from literature review. This genetic factor according to (Ilo, 2022) 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 (Ilo, 2022). This established the range as

$$\varepsilon = 0 \leq \varepsilon \leq 1 \qquad (2)$$

ISSN 2393-8471

International Journal of Recent Research in Civil and Mechanical Engineering (IJRRCME)
Vol. 11, Issue 1, pp: (61-66), Month: April 2024 – September 2024, Available at: www.paperpublications.org

3. METHODOLOGY

Thermodynamic expressed infectivity model is incorporated in an adopted basic viral dynamics and the ensued model solved simultaneously with five different genetic factors, $\varepsilon = 0$; $\varepsilon = 2.0 \times 10^{-3}$; $\varepsilon = 3.0 \times 10^{-3}$; $\varepsilon = 6.0 \times 10^{-3}$ and $\varepsilon = 7.0 \times 10^{-3}$ within genetic factor range for the five series of move, black, green, blue and red respectively to x-ray implications of genetic factor in the dynamics of HIV infection. Historical data to quantify the expressed model were that of interfacial free energetics and genetics factor obtained from (Ani, 2016) and (Ilo, 2022) respectively. The adopted basic viral dynamics model, an Ordinary Differential Equation (ODE) and the solution of the ensued model from numerical integration that utilized explicit Runge-Kutta method is simulated for the infection time course using MATLAB™ function ode 23. The infection dynamics was allowed to progress from day zero to about 300 day for the first instance to x-ray the dynamics at equilibrium point and at the second instance to x-ray the initial oscillatory dynamics which is an acute consequence of genetic factor. The solution showed dynamics as expected.

HIV dynamics thermodynamics model

Incorporating the thermodynamically expressed infectivity parameter in the adopted model equation (1), the ensued equation (2) is utilised in the simulations.

$$\dot{x} = \lambda - dx - \varepsilon\left(\frac{\psi(\gamma_{PS})}{\gamma_{PL} + \gamma_{SL}}\right)xv,$$

$$\dot{y} = \varepsilon\left(\frac{\psi(\gamma_{PS})}{\gamma_{PL}+\gamma_{SL}}\right)xv - ay,$$

$$\dot{v} = ky - uv. \qquad (3)$$

Where γ_{SL}, γ_{PL} and γ_{PS} are interfacial energetics between susceptible cell and serum, virus and serum and virus and susceptible cell respectively.

4. RESULTS AND DISCUSSIONS

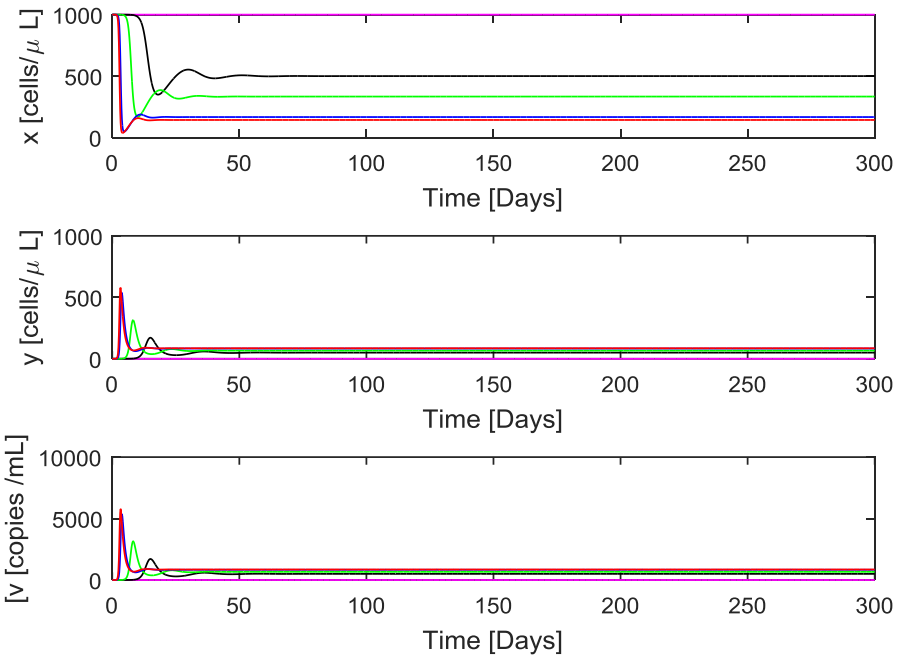

Fig 2: Five series of Infection dynamics progression to equilibrium due to five different genetic factors.

ISSN 2393-8471

International Journal of Recent Research in Civil and Mechanical Engineering (IJRRCME)
Vol. 11, Issue 1, pp: (61-66), Month: April 2024 – September 2024, Available at: www.paperpublications.org

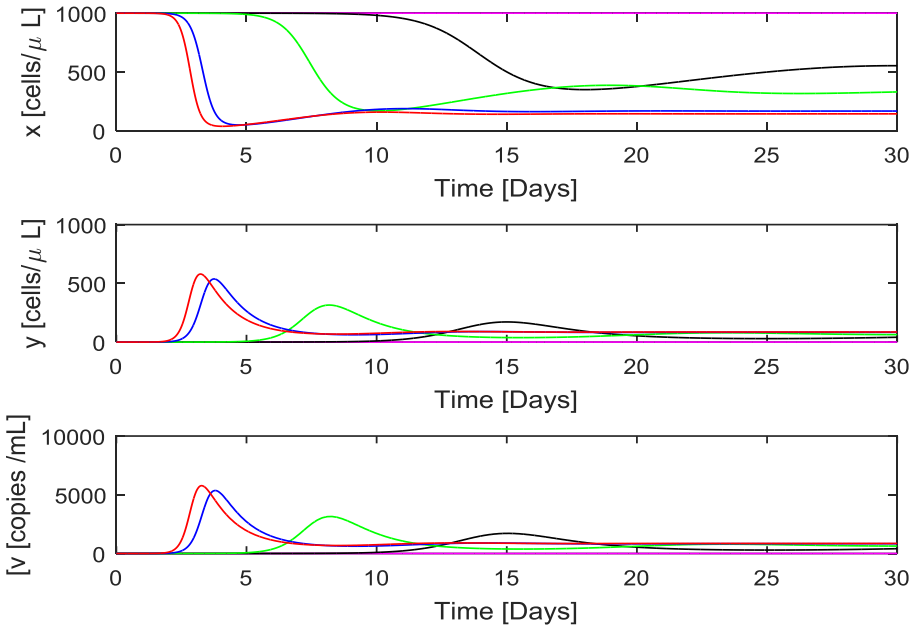

Fig 3: Five series of Infection dynamics acute oscillation due to five different genetic factors.

Figures 2 and 3 are quite informative based on the fact that they both display infection time course that are in agreement with the literature. Figure 2 and 3 show actually the effect of genetic factor to the infectivity value of the infection. Comparatively, the black series with $\varepsilon = 2.0 \times 10^{-3}$, the best genetic factor of all the series produced time course with the highest $CD4^+$ T cell count of about (350-499) cells per µL ($cells\mu L^{-1}$) as compared to the red series with $\varepsilon = 7.0 \times 10^{-3}$, the worst genetic factor produced time course with lowest $CD4^+$ T cell count of about (250-350) cells per µL ($cells\mu L^{-1}$). This goes a long to unravel the plethoria of infectivity in HIV dynamics. The uninfected cell $CD4^+$ T cell count for all the series is seen to be between two hundred and four hundred and ninety-nine (200-499) cells per µL ($cells\mu L^{-1}$) which is line with the literature which says that within the first eight years, uninfected cell $CD4^+$ T cell count is between two hundred and four hundred and ninety-nine (200-499) cells per µL ($cells\mu L^{-1}$). Again, the dynamics of acute stage of infection in figures 2 and 3, shows expected oscillation in all the subplots. The oscillatory dynamics is as a result of initial vigor by the genetic factor trying to battle down the infection while the infection driving parameter tries to resist the action of the genetic factor hence the oscillation. One thing is worthy of note, and that is the fact that the genetic factor zero that gave infectivity value of $0\left({}^{mL}/_{copies.d}\right)$ was able to resist the infection as seen in series with move colour with the uninfected cell count maintained a constant value 1000 cells per µL ($cells\mu L^{-1}$) while in other vales of genetic factors that made the infected cells susceptible, the infection progressed as expected.

The result of this paper explains the fact that there is plethoria of infectivity in HIV dynamics hence the need for a therapeutic approach that takes cognizance of individual genetic factor. The application of this study in pharmaceutical industries, in the area of drug design and in clinical studies cannot be overemphasized.

REFERENCES

[1] Anacleto, O., Cabaleiro, S., Villanueva, B., Saura, M., Houston, R., Woolliams, J., & Doeschl-Wilso, A. (2019). Genetic differences in host infectivity affect disease spread and survival in epidemics. *Scientific Reports* 9:4924 https://doi.org/10.1038/s41598-019-40567-w.

[2] Ani, O. I., (2016). *Surface energetics study of the interactions between HIV and blood cells treated with antiretroviral drugs.* Ph.D dissertation, mechanical engineering department, Nnamdi Azikiwe University, Awka.

[3] Bonhoeffer, S., May, R.M., Shaw, G.M. & Nowak, M.A, (1997). Virus dynamics and drug therapy. *Proc of the National Academy of Science of the United States of America, PNAS, Medical Sciences* 94(13): 6971-6976.

[4] Ganusov, V. V., Neher, R. A., & Perelson, A. S. (2013). Mathematical modeling of escape of HIV from cytotoxic T lymphocyte responses. *J. Stat Mech*. 2013: P01010–. doi:10.1088/1742-5468/2013/01/P01010.

[5] Hill, A. L., Rosenbloom, D. I. S., Nowark, M. A. and Siliciano, R. F.(2018). Insight into treatment of HIV infection from viral dynamics models, *Immunological Reviews*, 285, 9-25, John Wiley & Sons Ltd.

[6] Ilo, C. P., Omenyi S. N., and Dim, E. C. (2021a). "Genetic factor simulations for HIV infectivity in viral dynamics." *Journal of Engineering and Applied Sciences (JEAS)*, volume 19, number 1, pp 436-450.

[7] Ilo, C. P., Omenyi S. N., and Ani, O. I. (2021b). "Quantifying drug primary mechanism of action parameter in HIV (viral) Dynamics." *Journal of Engineering and Applied Sciences (JEAS)*, volume 19, number 1, pp 615-624.

[8] Ilo, C. P. (2024a). Thermodynamics of genetic transcriptional bifurcation in HIV Dynamics via computational technique. *Digital Innovation and Disruptive Technologies Towards: Towards Achieving a Digital Nation, 1st International Conference/Homecoming of ESUT CEE Alumni, June 26-28.*

[9] Ilo, C. P. (2024b). Electrostatics-Thermodynamics Adhesion in HIV with $CD4^+$ T Cell Dynamics. *Innovation in Electrical and Electronic Engineering for Sustainable Development, 1st International Conference/Homecoming of ESUT EEE Alumni, July11-12.*

[10] Ilo, C. P. (2022). *Surface Thermodynamics of infectivity in HIV viral dynamics.* PhD dissertation, Nnamdi Azikiwe University.

[11] Jeffry A. M. (2006). *A control theoretic approach to HIV/AIDS drug dosage design and timing the initiation of therapy*. PhD dissertation, University of Pretoria. Available [online]: http://www.upetd.up.ac.za/thesis/available/etd-12152006-104428/.../02chapter3.pdf.

[12] Omenyi, S. N. (2005). The concept of negative hamaker coefficient. Nnamdi Azikiwe University, Awka, *Inaugural Lecture Series* No. 8, 1, p.23

[13] Nettleman, M. D. and David, G. E. (2021). HIV Tests, Symptoms, Signs and Stages of HIV Infection. C. P. Davis (Ed), *medicinenet.* www.medicinenet.com.

[14] Perelson, A. S. & Nelson, P. W., (1999). Mathematical analysis of HIV-1 dynamics in vivo. *SIAM Rev*. 41(1), 3-44

[15] Santoro, M. M.and Perno, C.F. (2013) HIV-1 genetic variability and clinical implications. *ISRN Microbiol.* 2013:481314 10.1155/2013/481314

[16] Trevors, J. T. and Saier, M. H. Jr. (2011). Thermodynamic perspectives on genetic instructions, the laws of biology, diseased states and human population control, *C R Biol.* January; 334(1): 1–5. doi:10.1016/j.crvi.2010.11.008. Available in PMC 2014 July 10.

[17] Witten, G.Q., and Perelson, A.S., (2004). Modelling the cellular-level interaction between the immune system and HIV. *South African Journal of Science*, 100, 447-451.