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THERMODYNAMICS OF IMMUNITY WITH TRANSITION ADHESION COEFFICIENT IN HIV DYNAMICS

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Abstract: **Expressed and quantifiable thermodynamic adhesion coefficient representing HIV infectivity was incorporated in an adopted basic viral dynamics and thermodynamic model which is an Ordinary Differential Equation (ODE) was solved the with value of genetic factor when basic reproduction number was one at the first instance for condition of early infection and at the second instance for dynamics of later infection to show how genetic factor representing immune system fights off the disease even there was no therapeutic intervention for twenty days and four thousand days respectively. The solution approach of the Ordinary Differential Equation (ODE) was numerical integration that utilized explicit Runge-Kutta method in MATLAB^{TM} function ode 23. Historical data for the expressed adhesion coefficient was imported from relevant literature. Solutions of the of the model, that is uninfected cell (CD4+) count (x) ($cells\mu L^{-1}$), infected cell count (y) ($cells\mu L^{-1}$) and viral load (v) ($copies mL^{-1}$) infection time-course of dynamics of the thermodynamics model for 20 days for the first instance and 4000 days for second instance are in line with expectation. At the first instance which is dynamics at early stage shows that as the infection was established, the viral load picked with a corresponding drop of uninfected cell count with the expected absence of the infection oscillatory dynamics due to transition condition where every dynamic is expected to maintain an equilibrium immediately infection is established. At a later stage of the infection seen in in the second instance, it is amazingly evident that even without drug intervention, the infection was being fought down by the genetic factor in the proposed model. This is clearly seen where both viral load and infected cell count kept going down, owing to the fact that genetic factor is activating the cytotoxic T lymphocytes CTL killings of the infected cells hence viral load thereby reducing their count. Uninfected cell count as expected was seen to be approaching thymus supply rate ($x \cong {}^{\lambda}/_{d}$) approximately 1000($cells\mu L^{-1}$), increasing steadily even without any drug intervention which is in line with the principle. This is a clear indication of genetic factor in the model at work. The result of this paper is in line with the principle, hence validate the concept of genetic factor in the expressed adhesion coefficient model and providing understanding to infection dynamics without drug intervention. The result is of very importance to clinicians and in drug formulation.**

Keywords: **Human immunodeficiency virus, Interfacial energetics, Infectivity, van der Waals.**

1. INTRODUCTION

Although the burden of the epidemic continues to vary considerably between countries and regions an estimated 0.6% (0.6-0.7%) of adults aged 15-49 years worldwide are living with HIV. Again, 39.9 million (36.1-44.6) people were living with HIV at the end of 2023 (WHO, 2024). UNAIDS, (2013) documented that the solutions for the global increasing rate of Human Immunodeficiency Virus **(**HIV) infection are continuously being sought for, for its elimination. 88. 4 million (71-3-112.8million) people have been infected with the HIV virus and about 42.3 million (35.7-51.1) million people have died of HIV since the beginning of the epidemic (WHO, 2024). Variability in response to therapy has made some

individuals experience virologic failure on therapy that is highly effective on others. . About ten billion new viral particles of HIV can be generated daily, in chronic cases (Omenyi, 2005). Virus infectivity in HIV infection is observed to vary (Ganusov, Neher & Perelson, 2012).

Ani, (2015) through the study of interfacial energetics been established that the lymphocyte is the target of the virus. Ilo, (2022) through thermodynamics spectrophotometry gave an insight control infectivity in HIV dynamics. To unravel the mystery of transcriptional bifurcation in HIV dynamics (Ilo, 2024a) had developed a validated model through concepts of thermodynamics implementation. Ilo, (2024b) had also established HIV adhesion driven infectivity through electrostatics interaction mechanism. 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. All these successes formed the decision to x-ray dynamics of HIV infection at basic reproductive through thermodynamics.

2. PREVIOUS WORK/LITERATURE SURVEY

Functional Genetic Instructions (FGI)

To instruct cells how to assemble into living organisms achieved by absorption of energy, living organisms are programmed by functional genetic instructions (FGIs) which flow through a biochemical communication pathway involving DNA –RNA- proteins. 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. The most fundamental of all laws—the laws of thermodynamics govern all cells and subsequent species construction, since every known life form depend on having the correct FGIs maintained in their cells (Trevors and Saier, 2011).

Genetics factor in Adhesion coefficient.

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, (Anacleto *et al.*, 2019), opined that there is a direct evidence for genetic variation in host infectivity. Ilo, (2022), stated that the infection driving parameter (adhesion coefficient parameter) Ω which represent the strength of adhesion to the susceptible cell by the infectious agent and resistance due to thermodynamic genetic factor ε have been established as a function of infectivity in HIV dynamics.

$$\beta_{0T} = f(\varepsilon\Omega) \tag{1}$$

Using interfacial energetic, the adhesion coefficient was modelled as

$$\beta_{0T} = \varepsilon\left(\frac{\psi(\gamma_{PS})}{\gamma_{PL}+\gamma_{SL}}\right) \qquad (0 \leq \varepsilon \leq 1) \tag{2}$$

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 and ψ static dynamic factor.

Cytotoxic T lymphocytes (CTL) and Immune responses in absence of drugs

From Lai, (2014), cytotoxic T lymphocytes (CTL) and some neutralising antibodies respectively can help in clearing the infected cells and free virus as it was also observed that the basic model can be extended to consider immune responses. Many infected cells may be killed by CTL before they can produce large amounts of virus in individuals with strong CTL responses, (Bonhoeffer, *et al.*, 1997; Yang, *et al.*, 1996). A little percentage of cells that escape from CTL killings produces most of the plasma virus. They are after about two days killed by viral cytopathicity. On the other hand, in a weak immune response individual, most infected cells may escape from CTL-mediated lysis, produce free virus and die after two days. The rate of CTL expansion is simply proportional to the amount of antigen. This implies that provided that there are antigens, the CTL response never goes extinct. Wordaz and Krakauer, (2000); Wordaz and Nowak, (2000) expressed that by lylic machanisms, CTL is assumed to kill infected cells which also function by decreasing the rate at which uninfected target cells become infected (Wodaz, Christensen, J. P. and Thomsen., 2002).

$$\frac{dx}{dt} = \lambda - dx - \left(\frac{\beta}{1+qz}\right)xv$$

$$\frac{dy}{dt} = \left(\frac{\beta}{1+qz}\right)xv - ay \tag{3}$$

The term qz represents the suppression/inhibition by CTL on the viral infection and reduction in viral production by immune response, (Wodarz and Nowak, 2000). 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 probability of infection (adhesion coefficient), a is death rate of infected cells, k is rate of virus production and u is clearance rate of virus particles.

Above immune model was given birth to by earlier basic viral dynamics model by other famous researchers, worthy to mention is that of (Bonhoeffer, *et al.*, 1997), which established that

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

A solution of model (3) was provided by (Hill et al, 2018) where three (3) main stages, namely the acute HIV infection (primary infection), asymptomatic and the advanced – aids are clearly shown in a typical HIV infection course of figure 1.

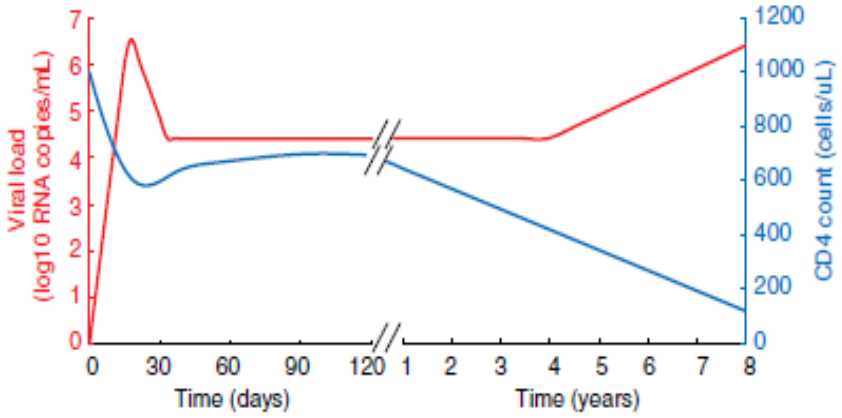

Figure 1: Approximate Time-Course with CD4 Count and Viral Load Estimates (Hill et al, 2018)

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.

Basic reproductive number

Bonhoeffer, *et al.*, (1997), maintained that the basic reproduction number R_0 is defined as average number of newly infected cells produced from any one infected cell. It is a term that describes the expected number of infections generated by one case in a susceptible population. If most cells are uninfected, x approximates $(x = {}^{\lambda}/_{d})$. R_0 is expressed as

$$R_0 = \frac{\lambda\beta k}{dau} \qquad (5)$$

At transitional, $R_0 = 1$, therefore equation 2.50 is obtained thus,

$$\frac{\lambda\beta k}{dau} = 1 \qquad (6)$$

3. METHODOLOGY

Expressed and quantifiable thermodynamic adhesion coefficient representing HIV infectivity by (Ilo, 2022), was incorporated in an adopted basic viral dynamics and the ensued thermodynamic model which is an Ordinary Differential Equation (ODE) was solved the with value of genetic factor when basic reproduction number was one at the first instance for condition of early infection and at the second instance for dynamics of later infection to show how genetic factor representing immune system fights off the disease even there was no therapeutic intervention for twenty days and four thousand days respectively. The solution approach of the Ordinary Differential Equation (ODE) was numerical integration that utilized explicit Runge-Kutta method in MATLAB™ function ode 23. Historical data for the expressed adhesion

coefficient was imported from relevant literature. Results of each sub-plot, that is uninfected cell (CD4+) count (x) ($cells\mu L^{-1}$), infected cell count (y) ($cells\mu L^{-1}$) and viral load (v) ($copiesmL^{-1}$) infection time-course of dynamics equation (7) for 20 days for the first instance and 4000 days for second instance are in line with expectation. They validate the concept and principles of genetic factor in the expressed adhesion coefficient.

HIV infection Thermodynamic model

Model equation (7) resulted when adhesion coefficient was introduced to adapted model (4). Model (7) was utilised in the simulation.

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

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

$$\dot{v} = ky - uv. \qquad (7)$$

4. RESULTS AND DISCUSSIONS

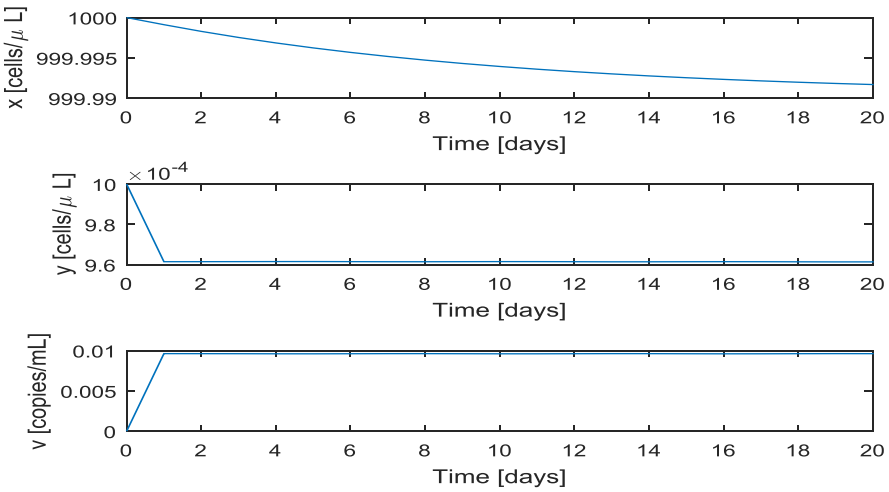

Fig 2: Simulation with transitional genetic factor at infection early stage.

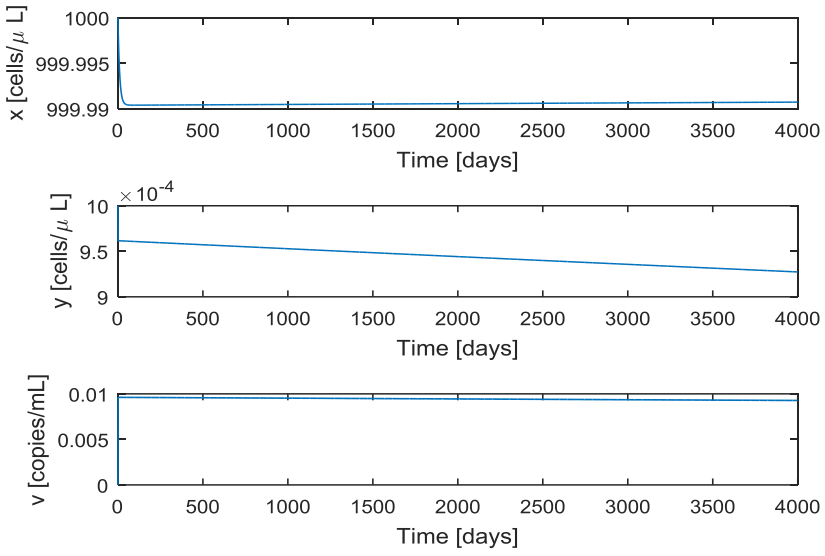

Fig 3: Simulation with transitional genetic factor till infection later stage.

Solutions of the of the model show infection time course are in line with expectation. Figure 2 which is dynamics at early stage shows how the infection was established where the viral load picked with a corresponding drop of uninfected cell count. The usual oscillatory dynamics of the infection was not experienced because the dynamics is at the transitional condition where every dynamic is expected to maintain equilibrium constant from the infection onset, but for the effects of genetic factor still at transition some changes were observed. At a later stage of the infection seen in figure 3, it is evident that even without drug intervention, the infection was being fought down by the genetic factor in the proposed model. This is clearly seen where both viral load and infected cell count kept going down, owing to the fact that genetic factor is activating the CTL killings of the infected cells hence viral load thereby reducing their count. Uninfected cell count was seen to be approaching ($x \cong {}^{\lambda}/_{d}$) approximately 1000($cells\mu L^{-1}$), increasing steadily even without any drug intervention which is in line with principle. This is clear indication and validation of genetic factor value at basic reproduction number of one in the model. The result of this paper is in line with principle hence validate the genetic factor introduced in the model.

Results of the of the study provides understanding to dynamics of infection without drug intervention. It helps in understanding infection progression. It is also helpful in the drug formulation.

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