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# DYNAMICS OF INTERFACIAL ENERGETICS AND FUNCTIONAL GENETICS IN HIV DISCORDANT COUPLES

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***Abstract:*** **Thermodynamic HIV infectivity expressed model was incorporated in an adopted basic viral dynamics model. The ensued thermodynamic HIV dynamic model, an Ordinary Differential Equation (ODE) was solved using the numerical integration that utilized explicit Runge-Kutta method in MATLAB™ function ode 23 for the infection time course of a HIV discordant couple. The infection dynamics representing the solution of the ensued model was allowed to progress from day zero to day one hundred and ninety nine in two series, the green series with $\varepsilon = 0$ representing infection dynamics of the HIV negative wife while the black series with $\varepsilon = 0.003$, represent the HIV positive husband with daily introduction of infected cells to the green series (woman) with introduction of infected cell count $y_{(1-199)} = 10^{-1}(cells\mu L^{-1})$ representing sex with the HIV positive man in black series. In the second instance some measure of control was introduced in the black series representing the man at day 200 to actually showcase that the dynamics can actually be influenced by drug intervention. Dynamics of the green series, the HIV negative wife remained uninfected despite introduction of infected cells $y_{(1-199)} = 10^{-1}(cells\mu L^{-1})$ representing sex with the HIV positive man in black series. The infectivity value at $\varepsilon = 0$ was obtained as $0\left(mL/_{copies.d}\right)$. This ensured that the green series being HIV negative woman did not get infected despite being the higher mass recipient during sex. The infection time course of the two series represented in principle what is expected in reality. This goes a long way to demystify the mystery of existence of HIV discordant couples. Means of characterizing the genetic factor in HIV infectivity should be sought in further studies to give it a physical meaning as its use can actually hinder continued HIV infection.**

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

## 1. INTRODUCTION

WHO, (2024) noted that with an estimated 0.7% (0.6-0.8%) of adults aged 15-49 years, although the burden of the epidemic continues to vary considerably between countries and regions world HIV population as at the end of 2022 stood at average of 39.0 million people with a range of (33.1-45.7 million people). Hill *et al*., (2018), noted that HIV, being one of the most intensively studied viral infections, has massive drug development efforts starting soon after identification of the virus with twenty seven (27) different antiretroviral drugs capable of halting viral replication and preventing transmission and progression to AIDS but still without a cure. As of December 2012, an estimated 9.7 million people in

low- and middle-income countries were receiving antiretroviral therapy, an increase of 1.6 million over 2011, (UNAIDS, 2013). Piot, (2005) noted that AIDS as a complex set of problems-requiring a combination of solutions should be considered as an issue that is at par with climate change and extreme poverty and that it should no longer be considered as just one of the numerous public health problems. Due to gaps in HIV services, 770 000 people out of approximately 37.9 million people living with HIV died from HIV related causes with 1.7 million people newly infected at the end of 2018, (WHO, 2019). Reduction of HIV related morbidity and mortality, restoration and/or preservation of immunologic function, maximal and durable suppression of the viral load, and subsequent improvement of quality of life are the primary goals of an effective therapy regimen (US Department of Health and Human Services, 2005; Jeffry, 2006).

Immunology and viral dynamics which entails the use of mathematical models to predict the infection dynamics with the infected have been of immense help. Bonhoeffer *et al*., (1997) gave a basic model, equation (1) that has served as a good tool in the analysis.

$$\begin{aligned} \dot{x} &= \lambda - dx - \beta xv, \\ \dot{y} &= \beta xv - ay, \\ \dot{v} &= ky - uv. \end{aligned} \tag{1}$$

Where $x$ is susceptible cells, $y$ is infected cells, $v$ is virus particle, $\lambda$ is rate of production of susceptible cells, $d$ is death rate of susceptible cells, $\beta$ 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.

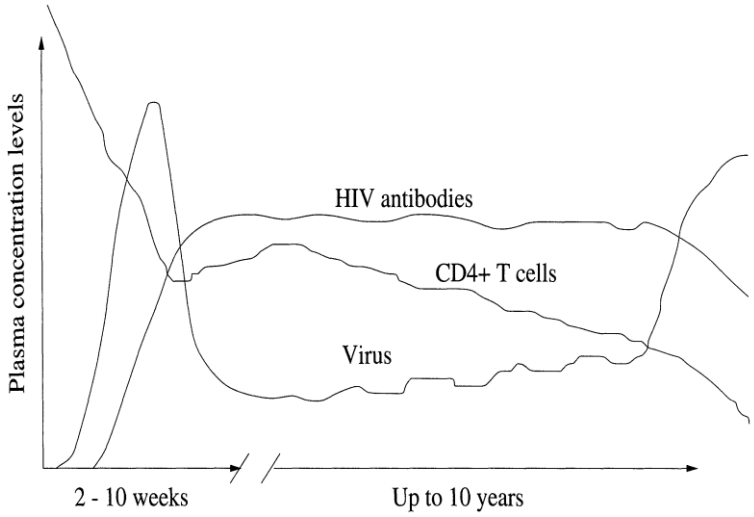


**Figure 1: Approximate Time-Course of HIV Infection, (Witten and Perelson, 2004; Perelson and Nelson, 1999).**

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.

The new field of viral dynamics, based on within-host modelling of viral infections, began with models of human immunodeficiency virus (HIV), but now includes many viral infections (Geetha, and Balamuralitharan, 2018). Many of the models emphasized quantitative findings about HIV biology uncovered by studying acute infection, the response to drug therapy and the rate of generation of HIV variants that escape immune responses. Some of these models have revealed many dynamical features of HIV infection and how it may provide insight into the ultimate cure for this infection, (Perelson and Ribeiro, 2013).

Construction of first cells, and all subsequent species, 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. All known life forms depend on having the correct FGIs maintained in their cells. Again, 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. 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. Lastly, Ilo, (2024b) had also established HIV adhesion driven infectivity through electrostatics interaction mechanism.

In this paper, genetic factor in infectivity explains thermodynamically the discordance in HIV discordant couples.

## 2. PREVIOUS WORK/LITERATURE SURVEY

**Genetics and interfacial energetics in HIV dynamics**

The strength of adhesion to the susceptible cell by the infectious agent (the infection driving parameter) $\Omega$ and resistance due to thermodynamic genetic factor ε have been established by (Ilo, 2022) as a function of infectivity in HIV dynamics. Again, 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.

$$\beta = \int(\varepsilon\Omega) \tag{2}$$

The implication is that the infection (fusion) of a HIV particle to a lymphocyte is enabled or driven by adhesion of HIV unto CD4 receptor against a resistive genetic factor. Further, the disease progression which means susceptibility HIV is respectively inhibited by the resistance due to genetic factor, ε (where $0 \leq \varepsilon \leq 1$). From literature, functional thermodynamic genetic instructions (FGIs) at optimum performance produce a value of $\varepsilon = 0$.

Bearing in mind the numerical static-dynamic factor $\psi$, since the data were obtained under static condition where blood in the circulatory system is in constant motion (Ilo,2022)

$$\beta = \varepsilon\left(\frac{\psi(\gamma_{PS})}{\gamma_{PL}+\gamma_{SL}}\right) \tag{3}$$

The component terms of (3) are approximately expressed as follows,

$$\gamma_{SL} \cong \sqrt{\gamma_S\gamma_L} \tag{4}$$

$$\gamma_{PL} \cong \sqrt{\gamma_P\gamma_L} \tag{5}$$

$$\gamma_{PS} \cong \sqrt{\gamma_P\gamma_S} \tag{6}$$

$\psi$ static dynamic factor being equal to 0.1 according to Chazal, *et al.* (2014),

$\gamma_L$ is the surface free energy of serum (infected),

$\gamma_S$ is the surface free energy of lymphocytes (uninfected lymphocytes),

$\gamma_P$ is the surface free energy of HIV (infected lymphocytes).

Geometric mean value expression of (4) to (6) is applied to get the interfacial free energies$\gamma_{SL}$, $\gamma_{PL}$ and $\gamma_{PS}$.

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## 3. METHODOLOGY

This study involved incorporating expressed thermodynamic infectivity model in an adopted basic viral dynamic. The ensued model is solved simultaneously with two different values of genetic factor $\varepsilon = 0$, for green series representing HIV negative woman and $\varepsilon = 0.003$, for black series representing HIV positive man with daily introduction of infection to the green series (woman) with introduction of infected cells $y_{(1-300)} = 10^{-1}(cells\mu L^{-1})$ representing sex with the HIV positive man in black series. 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 simulated for the infection time course using MATLAB™ function ode 23. The infection dynamics was allowed to progress from day zero to about 200 day on the first instance while in the second instance some measure of control was introduced in the black series representing the man from day 200 to day 300. The solution showed dynamics as expected both in the first instance and in the second instance during some measures of control.

**HIV dynamics thermodynamics model**

Incorporating the thermodynamically expressed infectivity parameter in the adopted model equation (1), the ensued equation (7) is utilised in the simulations.

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

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

$$\dot{v} = ky - uv. \tag{7}$$

## 4. RESULTS AND DISCUSSIONS

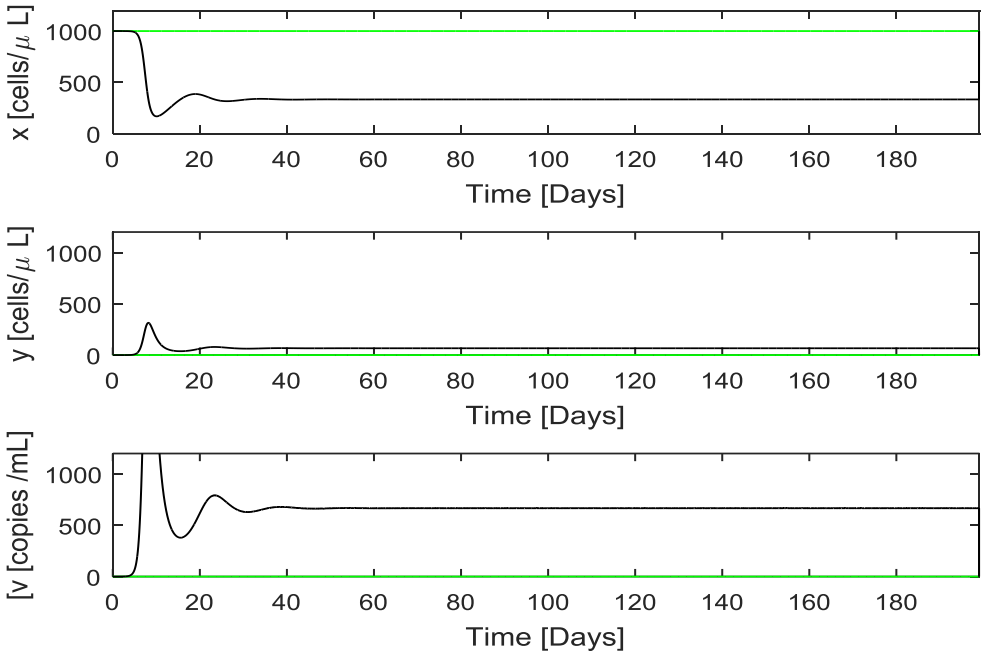


**Fig 2: Infection dynamics with discordant couple having sexual relationship without drug intervention.**

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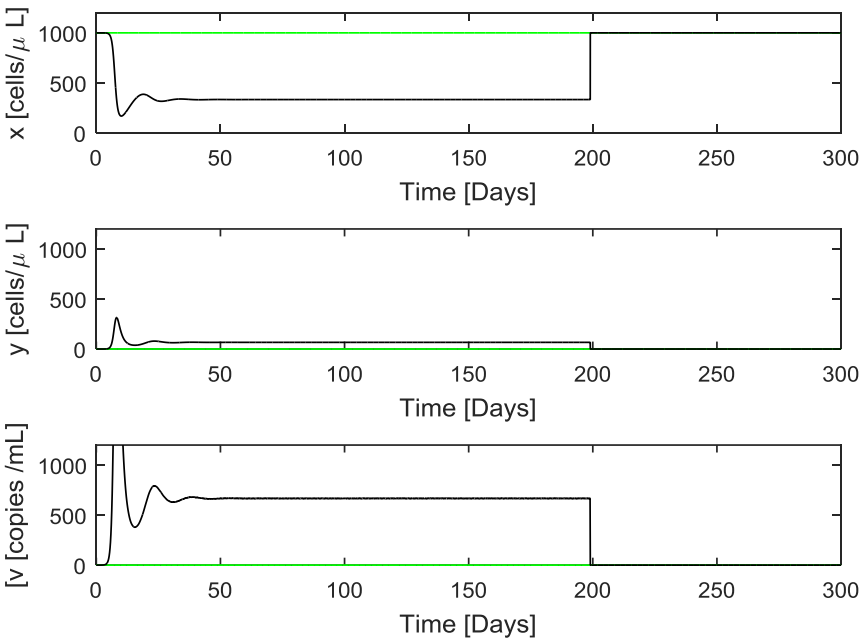


**Fig 3: Infection dynamics with discordant couple having sexual relationship with efficient drug intervention at day 200**

Expression and quantification of thermodynamic infectivity values are in line with the historical data. At the first instance figure 2, the genetic factor $\varepsilon = 0$ the infectivity value became $0\left({}^{mL}/_{copies.d}\right)$. With value of infectivity being $0\left({}^{mL}/_{copies.d}\right)$, it is impossible for infection to be achieved, hence infection was not achieved. This is why even with daily inoculation (sex) of the green series (the HIV negative woman) with some dose of infected cell from the black series, the husband (the HIV positive man) to a high tune of $y_{(1-300)} = 10^{-1}(cells\mu L^{-1})$, the green series (the HIV negative woman) remained negative to HIV and uninfected through-out the infection time course. In the second instance, to show that to show actually that the black series represents actual HIV infection dynamics, some measures of control with high efficacy was introduced at day 200 and there was a marked change in the dynamics which shows a curative trend.

At optimum functional thermodynamic genetic instructions (FGIs) for either of a couple, $\varepsilon = 0$. What explains discordant couples is optimum functional thermodynamic genetic instructions (FGIs). This means that the black series in the plot which represents HIV positive husband can not by help of optimum functional thermodynamic genetic instructions (FGIs) infect the green series which represents the HIV negative wife. This result demystifies HIV discordance in couples living together as husbands and wives and having unprotected sexual relationships.

An option of preventing or counteracting HIV-blood interaction could be achieved by application of this result if there should be some sort of genetic enhancement to meet up with the requirements of functional thermodynamic genetic instructions (FGIs) at optimum performance. The application of this study in pharmaceutical industries, in the area of drug design and in clinical studies cannot be overemphasized.

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