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Predictability Analysis on HIV/AIDS System using Hurst Exponents

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***Abstract*—**Methods of contemporary mathematical physics such as chaos theory are useful for analyzing and understanding the behavior of complex biological and physiological systems. The three dimensional model of HIV/AIDS is the basis of active research since it provides a complete characterization of disease dynamics and the interaction of HIV-1 with the immune system. In this work, the behavior of the HIV system is analyzed using the three dimensional HIV model and a chaotic measure known as the Hurst exponent. Results demonstrate that Hurst exponents of CD4, CD8 cells and viral load vary nonlinearly with respect to variations in system parameters. Further, it was observed that the three dimensional HIV model can accommodate both persistent (H>0.5) and anti-persistent (H<0.5) dynamics of HIV states. In this paper, the objectives of the study, methodology and significant observations are presented in detail.

***Keywords*—**HIV/AIDS, mathematical model, chaos theory, Hurst exponent

I. Introduction

THE mathematical models used to represent the dynamics of infectious diseases can explain highly complex clinical signals and symptoms. It is in the context of modeling, that scientists and technologists can apply their knowledge to formulate guidelines for clinical tests and practical measurements [1,2]. Mathematical modeling of the interaction between HIV-1 and the immune system improves the understanding of the dynamics of the disease [3]. Many HIV dynamic models have been proposed by researchers [4-8] to provide theoretical principles for development of treatment strategies for HIV infected patients [9].

The nonlinear three dimensional HIV model is the basis of active research [1] since it includes most aspects known thus far regarding the dynamics of HIV-1 in the human body [3]. Since all parameters of this model can be determined from CD4 cell levels and viral load in blood, the three dimensional model is highly useful for practical applications [10]. This model can be used to simultaneously obtain the response of the CD4 lymphocyte population, the CD8 lymphocyte population and the HIV-1 viral load and permits an analytical study of the dynamics of the disease. The model can also be used to determine the state of health of an individual and verify the effects of drugs [3]. The analysis of complexity of the HIV model is essential for choosing proper parameter estimation methods and for designing suitable control strategies.

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The nonlinear analysis on HIV models is critical to explore viral fitness assays and estimate viral fitness parameters [11]. There are several reports regarding the nonlinear analyses on models describing HIV dynamics. Bortz and Nelson (2004) [12] performed a formal sensitivity analysis on a nonlinear model of HIV infection dynamics and presented the results of both a differential analysis as well as a principle component based analysis. David *et al*. (2008) [13] performed sensitivity analysis on a nonlinear HIV model using both classical sensitivity functions and generalized sensitivity functions. Naresh *et al*. (2009) [14] performed numerical analysis on a nonlinear HIV model to investigate the influence of certain key parameters on the spread of the disease.

Ye and Ding (2009) [15] introduced fractional order into an HIV model and analyzed its chaotic behavior using an Adams-type predictor-corrector method. Al-Sheikh *et al*. (2011) [16] performed stability analysis on a non-linear mathematical model which analyzes the spread and control of HIV. Lavielle *et al*. (2011) [17] used a maximum likelihood estimation algorithm, to analyze simultaneously the HIV viral load decrease and the CD4 increase in patients using a nonlinear HIV model. Further, Ho and Ling (2010) [18] have shown that the system dynamics of the three dimensional HIV model is sensitive to both the initial conditions and the system parameters. Hence, the HIV system is chaotic and exhibits a bifurcation behavior.

Methods of contemporary physics such as chaos theory are important for biological systems research [19]. Chaos and many regulatory mechanisms control the dynamics of living systems. These mechanisms are associated with the regulation of voltage-dependent ion channels, regulation of enzyme activity, the control of receptor activity or transport processes, viral dynamics and also circadian rhythms [20,21]. In analysis of bio-systems and process, different chaotic measures are used. Among such measures, calculating chaotic exponents such as Hurst exponents and dimensional analysis are most important and common [22].

The objective of this work is to extensively analyze the complexity of the HIV/AIDS system using the three dimensional HIV model and a nonlinear, chaotic measure known as the Hurst exponent.

II. Methodology

A. The three dimensional HIV model

The response of the concentrations of the CD4 lymphocyte population, the CD8 lymphocyte population and the HIV-1 viral load can be characterized by the following first order nonlinear differential equation [18, 23-25].

$$\frac{dx(t)}{dt} = a(x_0 - x(t)) - bx(t)z(t) \quad (1a)$$

$$\frac{dy(t)}{dt} = c(y_0 - y(t)) + dy(t)z(t) \quad (1b)$$

$$\frac{dz(t)}{dt} = z(t)(ex(t) - fy(t)) \quad (1c)$$

where, x(t), y(t) and z(t) are the concentrations of the CD4 lymphocyte population, the CD8 lymphocyte population and the HIV-1 viral load, respectively. x_0 and y_0 are the normal unperturbed concentrations of the CD4 and CD8 lymphocyte population. a, b, c, d, e and f are the system parameters. The description of each parameter [26] is provided in Table 1.

TABLE I
DESCRIPTION OF HIV MODEL PARAMETERS

Parameter	Description
a	death rate of CD4 cells
b	rate of infection of CD4 cells by virus
c	death rate of CD8 cells
d	rate of increase of CD8 cells in response to increased viral load
e	rate of increase of viral load
f	rate of decrease of viral load

B. Estimation of Hurst exponent

Hurst exponent (H) [27-29] is responsible for a measure of predictability of a time series. Hurst exponent values range between 0 and 1. A value 0.5 < H < 1 indicates persistent behavior where one can expect with increasing certainty that whatever direction of change has been current will continue. Values 0 < H < 0.5 indicates anti-persistent behavior, in that one can expect whatever direction of change is current is unlikely to continue. A straight line with non zero gradient would have a Hurst exponent of 1.

In this work, the Hurst exponents of CD4 cell population, CD8 cell population and HIV-1 viral load were calculated using the aggregated variance method [30-32]. Let $(X_t)_{t\in N}$ be a time series, shortly denoted by (X_t). For an integer m between 2 and N/2, the series is divided into blocks of length m and the sample average is computed over each k^{th} block.

$$\overline{X}_k^{(m)} = \frac{1}{m}\sum_{t=(k-1)m+1}^{km} X_t \ , \qquad k = 1, 2, ..., [N/m] \quad (2)$$

For each m, the sample variance of $\overline{X}_k^{(m)}$ is computed across the blocks

$$s_m^2 = \frac{1}{([N/m]-1)}\sum_{k=1}^{[N/m]} (\overline{X}_k^{(m)} - \overline{X})^2 \quad (3)$$

For successive values of m, the sample variance s_m^2 is plotted against m on a log-log plot. The estimate of H is the slope of the least squares line fit to the points of the plot.

III. RESULTS AND DISCUSSION

Figure1 shows the variation in the Hurst exponents of CD4, CD8 cell populations and HIV-1 viral load as a function of parameter 'a' in the range of 0 to 1. A nonlinear variation is seen in the Hurst exponent of CD4 cell population in the adopted range of parameter 'a'. The Hurst exponent of CD8 cells appear to decrease and then increase as the value of parameter 'a' is increased from 0 to 1. Further, only small variations in the Hurst exponent of viral load are seen as the value of parameter 'a' increases.

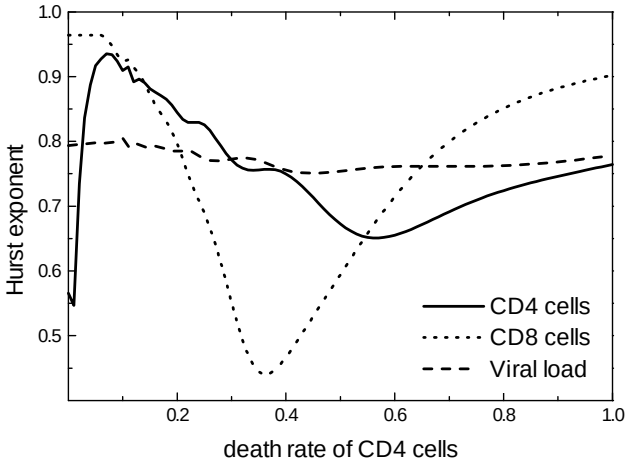

Fig. 1 Variation of the Hurst exponents of CD4, CD8 cell populations and HIV1 viral load shown as a function of parameter 'a'

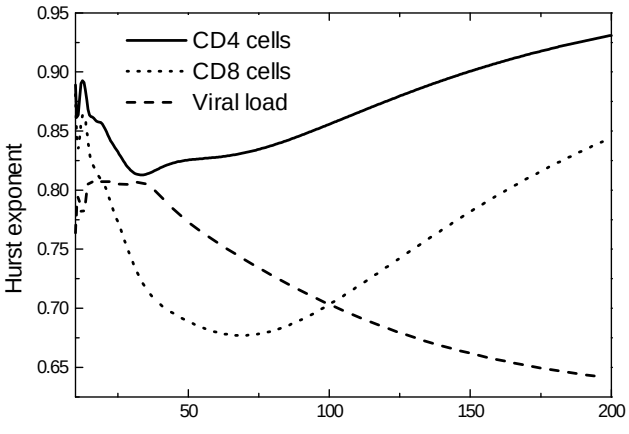

Fig. 2 Variation of the Hurst exponents of CD4, CD8 cell populations and HIV1 viral load shown as a function of parameter 'b'

Figure 2 shows the variation in the Hurst exponents of CD4, CD8 cell populations and HIV-1 viral load as a function of parameter 'b' in the range of 10 to 250. It is seen that the Hurst exponents of CD4 and CD8 cell population decreases and then increases as the value of parameter 'b' increases. Whereas, the Hurst exponent of viral load increases initially and further decreases exponentially as parameter 'b' increases.

The variation in Hurst exponents of CD4, CD8 cell populations and HIV1 viral load is shown as a function of parameter 'c' in Figure 3. The Hurst exponents of CD4 cells and viral load decreases almost linearly as the value of parameter 'c' increases in the range of 0 to 1. Further, a

nonlinear variation is seen in the Hurst exponent of CD8 cell population in the adopted parameter range.

The variation in Hurst exponents of CD4, CD8 cell populations and viral load is shown as a function of parameter 'd' in Figure 4. It is found that the Hurst exponents of CD4 and CD8 cells increase nonlinearly as the value of parameter 'd' increases in the range of 0 to 40. However, the Hurst exponent of viral load decreases in the adopted parameter range.

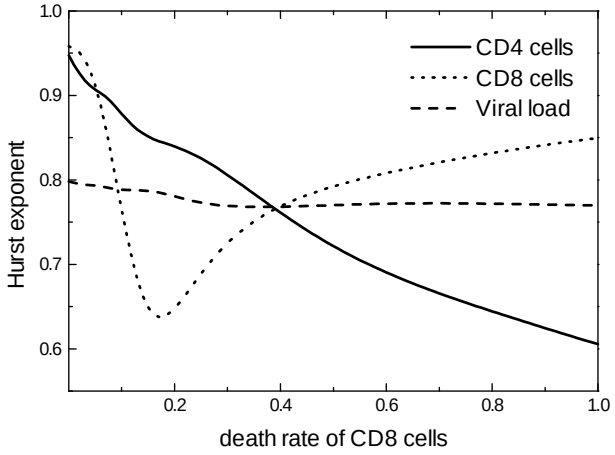

Fig. 3 Variation of the Hurst exponents of CD4, CD8 cell populations and HIV1 viral load shown as a function of parameter 'c'

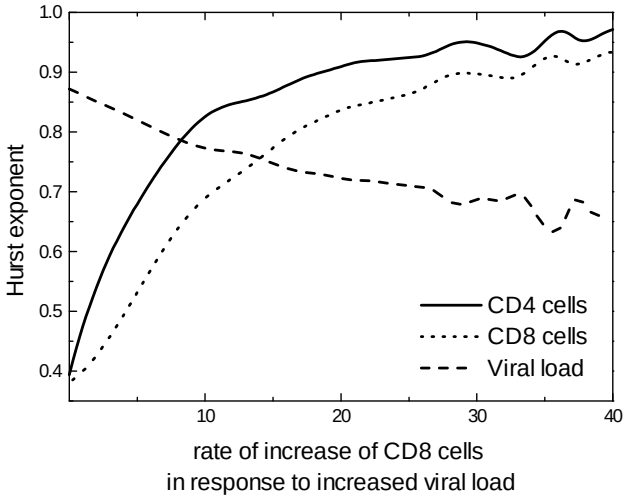

Fig. 4 Variation of the Hurst exponents of CD4, CD8 cell populations and HIV1 viral load shown as a function of parameter 'd'

Similarly, Figure5 shows the variation in the Hurst exponents of CD4, CD8 cell populations and HIV-1 viral load as a function of parameter 'e' in the range of 0 to 0.02. It is seen that the Hurst exponents of CD4 and CD8 cells decrease nonlinearly with increase in parameter 'e'. Also, a nonlinear variation is seen in the Hurst exponent of viral load in the considered range of parameter 'e'.

Figure 6 shows the variation in the Hurst exponents of CD4, CD8 cell populations and viral load as a function of parameter 'f' in the range of 0 to 0.03. The Hurst exponent of viral load appears to decrease as the value of parameter 'f' increases. However, the Hurst exponents of CD4 and CD8 cells are seen to vary nonlinearly in the adopted parameter range.

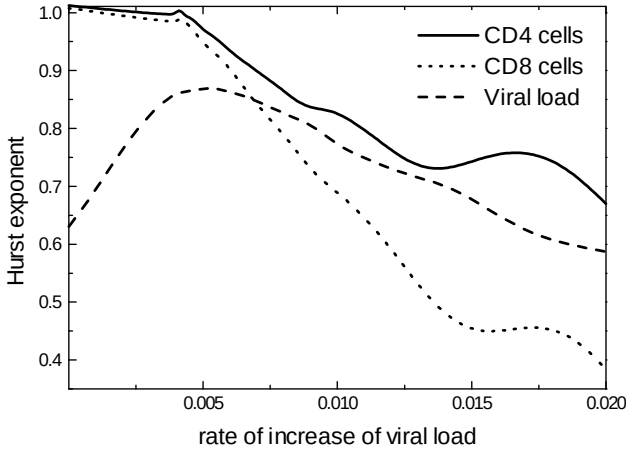

Fig. 5 Variation of the Hurst exponents of CD4, CD8 cell populations and HIV1 viral load shown as a function of parameter 'e'

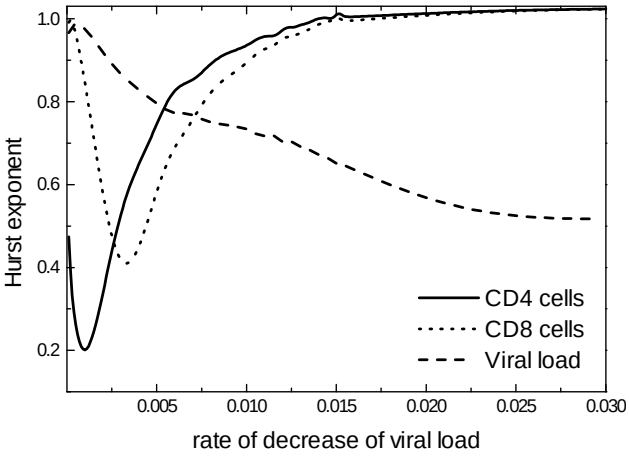

Fig. 6 Variation of the Hurst exponents of CD4, CD8 cell populations and HIV1 viral load shown as a function of parameter 'f'

Table II shows the parameter range and the corresponding behavior of CD4 cell population. It is found that the CD4 cell population exhibits persistent behavior (H>0.5) in the adopted range of parameters 'a', 'b', 'c' and 'e'. Anti-persistent behavior (H<0.5) in CD4 cells is seen in the case of parameters 'd' and 'f' in the range of 0-1.25 and 0-0.0028 respectively. It appears that the parameters 'd' and 'f' contribute to the anti-persistent behavior of CD4 cells.

Similarly, the parameter range and the corresponding behavior of CD8 cell population is shown in Table 3. The CD8 cell population is found to exhibit persistent behavior in the adopted range of parameters 'b' and 'c'. Anti-persistent behavior in CD8 cells is seen in the case of parameters 'a', 'd', 'e' and 'f' in the range of 0.32-0.42, 0-4, 0.0136-0.02 and 0.0024-0.0044 respectively. It is noted that the parameters 'a', 'd', 'e' and 'f' contribute to the anti-persistent behavior of CD8 cells.

Further, typical persistent and anti-persistent behavior of CD4 cell population is shown in Figures 7 and 8 respectively.

TABLE II
THE PARAMETER RANGE AND THE CORRESPONDING BEHAVIOR OF CD4 CELL POPULATION

Parameter	Parameter range	Behavior of CD4 cell population
a	0-1	Persistent
	-	Anti-persistent
b	10-200	Persistent
	-	Anti-persistent
c	0-1	Persistent
	-	Anti-persistent
d	1.5-40	Persistent
	0-1.25	Anti-persistent
e	0-0.02	Persistent
	-	Anti-persistent
f	0.0029-0.03	Persistent
	0-0.0028	Anti-persistent

TABLE III
THE PARAMETER RANGE AND THE CORRESPONDING BEHAVIOR OF CD8 CELL POPULATION

Parameter	Parameter range	Behavior of CD8 cell population
a	0-0.31, 0.43-1	Persistent
	0.32-0.42	Anti-persistent
b	10-200	Persistent
	-	Anti-persistent
c	0-1	Persistent
	-	Anti-persistent
d	4.25-40	Persistent
	0-4	Anti-persistent
e	0-0.0135	Persistent
	0.0136-0.02	Anti-persistent
f	0-0.0023, 0.0045-0.03	Persistent
	0.0024-0.0044	Anti-persistent

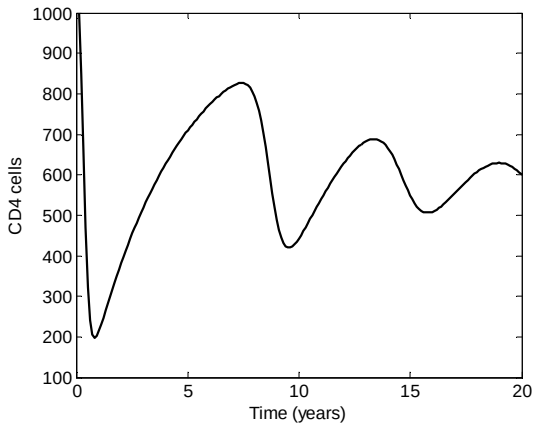

Fig. 7 A persistent behavior of CD4 cell population obtained using the three dimensional HIV model with a=0.25, b=50, c=0.25, d=10, e=0.01 and f=0.009

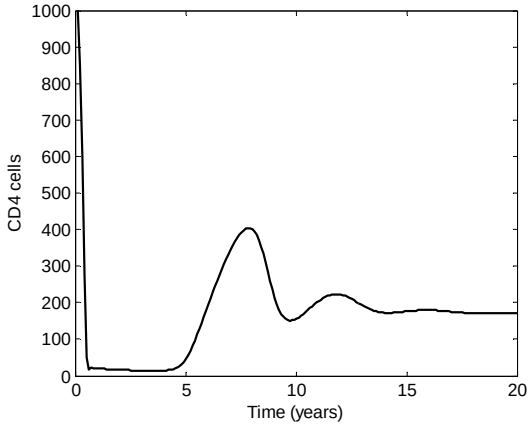

Fig. 8 An anti-persistent behavior of CD4 cell population obtained using the three dimensional HIV model with a=0.25, b=50, c=0.25, d=10, e=0.01 and f=10^{-6}

IV. CONCLUSIONS

A mathematical model that describes the dynamics of HIV infection is highly useful to decide on treatment strategies for HIV/AIDS patients [33]. The dynamic three dimensional HIV model is a commonly used model since it includes most aspects known thus far regarding the dynamics of HIV- 1 in the human body [3].

In this work, the complexity of the dynamic three dimensional HIV model has been analyzed using the Hurst exponent. The HIV model was simulated using Euler's method for different parameter values and the responses of CD4, CD8 lymphocyte populations and viral load were obtained. The Hurst exponents of the obtained states were calculated using the aggregate variance method.

Results demonstrate that Hurst exponents of CD4, CD8 cells and viral load vary nonlinearly in the adopted range of parameters 'a', 'b', 'c', 'd', 'e' and 'f'. Also, it was found that the three dimensional HIV model can accommodate both persistent and anti-persistent dynamics of HIV states. Further, the parameters 'd' and 'f' were found to contribute to the anti-persistent behavior (H<0.5) of CD4 cells. Whereas, the parameters 'a', 'd', 'e' and 'f' contribute to the anti-persistent behavior of CD8 cells. The viral load was found to exhibit persistent behavior in the considered range of parameters.

This study seems to be of high clinical significance since the analysis of complexity of the HIV model is essential for choosing proper parameter estimation methods and for designing suitable treatment strategies.

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