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# STATISTICAL TIME SERIES ANALYSIS FOR DYNAMICS OF HIV

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**Abstract**

$HIV$ has become global disease. These days a lot of people are suffering. Mostly $HIV$-positive people are not aware that they have been infected. Therefore, a strict check on donor blood and blood products have to be followed. Hence, it becomes important to interpret the chemical mechanism of $HIV$ infection and its spread. It infects a diverse range of immunity cells. It gets carried into the macrophages and $CD^{4+}T$ cells because of the communication among virion wrap glycoproteins with the $CD^4$ molecule on the target cells. These virions then infect a large amount of cellular targets and diffuse into every part of human body. Mathematical modeling for the mechanics of $HIV$ infection has been done to reduce its propagation, find cures for discourse. The model discussed in this paper consists of these states: $T$, number of cells not infected, $I$, number of cells infected, $V$, number of blood virus particles. The non-linear behavior for $HIV$ modelling is studied using time series analysis. Further, statistical tools like Regression, Correlation, Fractal dimension, Hurst Exponent, Predictability Index, Box plot etc. helps to understand the virion behavior in a better way. It is observed that as the state variables changed then the viral dynamics changes behavior from regular to chaotic.

**Keywords and phrases:** Time series, Statistical Analysis, Regular motion, Chaotic motion, $HIV$ dynamics.
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## 1 Introduction

Human Immunodeficiency Virus ($HIV$) represents the kind of virus that straightaway weakens the immunity of the body and leads to a life threatning infection called Acquired Immunodeficiency Syndrome ($AIDS$). It is a state where immune system gradually stops responding and allows the infection to grow rapidly. $HIV$ is a lentivirus that belongs to the family of retroviridae which causes chronic and lethal diseases. Lentiviruses are (+) positive-sense single-stranded $RNA$ ($+ssRNA$) viruses. They invade in the target cell to convert $RNA$ virus into $DNA$. This process of conversion from single-stranded $RNA$ to double stranded $DNA$ is called reverse transcriptase. The resulting $DNA$ virus then replicates inside the cell nucleus. Alternatively, the virus may reproduce new $RNA$ virus to restart the replication process. $HIV$ infection reduces the level of $CD^{4+}T$ cells. Patients are identified as $AIDS$ patients if the level of $CD^{4+}T$ cells reduces to a critical level of 200 cells per $mm^3$ or lower. Medicines forbid $HIV$ from increasing in the host tissues. This helps in reduction in the infection of $HIV$. Reverse Transcriptase Inhibitor ($RTI$) drugs are used for treatment

of $HIV$ infection. They block the process of reverse transcriptase which prevents the host cell from getting infected. Alternatively, Protease Inhibitor ($PI$) drugs are used to forbid the production of mature viruses at the end stage of the replication cycle.

Barunik J. *et al* [1] estimated hurst exponent for heavily tailed distributions. Beard J. *et al* [2] discussed economic level for life results of therapy for $HIV/AIDS$. Bhardwaj *et al* [3-5] studied various statistical characteristics of various real life phenomena of meditating body, to forecast weather, rainfall, environment data. Boshoff C.*et al* [6] discussed $AIDS$-related malignancies. Box G.E.P. *et al* [7] forecasted and controlled time series. Carbone A. *et al* [8] researched noise in various systems. Chu and Selwyn [9] discussed the complications of $HIV$ infection. Fuller W.A. [10] gave description of statistical time series. Grech D. *et al* [11] suggested techniques in detrended time series. Hurst H. *et al* [12] published a transaction on the rescaled analysis. Malta *et al* [13] described antiretroviral therapy for human immuno deficiency virus among drug users. Nicholas *et al* [14] studied managing symptoms, self-care for peripheral neuropathy in HIV/AIDS. Perelson and Nelson [15] discussed mathematical analysis of $HIV$-1 dynamics. Post and Holt [16] reviewed recent developments in $HIV$ and the kidney. Rangarajan and Ding [17] gave amalgamated access to the assessment of correlation in time series data. Samanta [18] discussed permanency and termination of a non-autonomous $HIV/AIDS$ epidemic model incorporated delay time. Walker [19] studied selected control of $HIV$ infection, its applications for vaccines. Wanga B.D. *et al* [20] suggested how vaccines and treatment can play a role in controlling $HIV$. Yarchoan R. *et al* [21] explained the influence of antiviral therapy on pathogenesis.

None of the authors have studied the time series, fractal and Hurst exponent analysis of $HIV$ model. This paper, studies impact of time on amount of uninfected cells; virus particles in the blood cells and infected cells. Also, time series, fractal dimension, Hurst exponent, predictability index and behaviour of these cells is observed.

## 2 Development of Mathematical Model

The mathematical model for the following three important components have been developed:

1. $T$, amount of uninfected cells,
2. $V$, amount of virus particles in the blood cells,
3. $I$, amount of infected cells.

The model helps to study the impact of $HIV$ epidemic on these factors simultaneously with time and also to study how the change in one component influences the changes in other with respect to time. Some assumptions that are required to transform the biological condition into a mathematical model are as follows:

1. Contact rate is being considered as a time varying function.
2. Reverse Transcriptase Inhibitor effect is being considered as a time varying parameter, $0 < \gamma < 1$.
3. Protease Inhibitor effect is being considered as a time varying parameter, $0 < \eta < 1$.
4. transmission system coefficient is considered a time varying parameter, $\beta$.

All parameters considered to be positive constants. Mathematical model can be generated considering the dynamics of $HIV$ infection

$$dT = (S - bT - (1 - \gamma)\beta TV)dt, \tag{2.1}$$

$$dV = ((1-\eta)NaI - cV)dt, \tag{2.2}$$
$$dI = ((1-\gamma)\beta TV - aI)dt, \tag{2.3}$$

with initial assumption: $T(0) = T_0$, $V(0) = V_0$, $I(0) = I_0$, where
$T$: measure of cells uninfected
$dT$: changing rate of uninfected cells
$S$: constant source rate producing $T$ cells
$b$: clearing rate of uninfected $T$ cells
Infection rate reduces from $\beta TV$ to $(1-\gamma)\beta TV$.
$V$: measure of blood virus particles
$dV$: changing rate of each cell infected producing the virus
$N$: average amount of virions produced by the cell infected over its life span
$a$: clearing rate of infected cells
$(1-\eta)NaI$: virions under affected by $PI$ drugs
$c$: rate at which virus are cleared
$I$: measure of infected cells
$dI$: changing rate in infected cells.

## 3 Methodology

### 3.1 Time Series Analysis

Time Series $\{x_t : t \in T\}$ is a collection of random variables usually parameterized by

- the real line $T = R = (-\infty, \infty)$,
- the non-negative real line $T = R^+ = [0, \infty)$,
- the integers $T = Z = \{..., -2, -1, 0, 1, 2, ...\}$,
- the positive integers $T = Z^+ = \{0, 1, 2, ...\}$.

*Univariate* time-series analysis is the investigation of a unary order of data whereas *multivariate* time-series analysis consists of various sets of data for the similar order of time intervals. Here, we have a multivariate time series for the analysis. The probability measure of a time series is defined by specifying the joint distribution (in a consistent manner) of all finite subsets of $\{x_t : t \in T\}$. There are two categories of statistics that describe data. First, explains the central position involving the mode, median, and mean. Second, measures of spread which consists of suming a group of data to describe the spread of the scores.

### 3.2 Rescaled Range Analysis

H.E.Hurst developed this scaling process. With time it was refined by Mandelbrot and Wallis. In this simulation, take the input of the time sequence measuring $T$. Divide these in $N$ equivalent time intervals measuring $\mu$, i.e. $N\mu = T$. Taking every time interval separately, calculate the average measure and construct new-sprung sequence of congregated deviations of mean. Then, range and standarddeviation of actual time sequence for every time interval, is measured. Standardise every range through related standarddeviation to form the rescaled range. Hence, the averagerescaledrange for the considered time intervals of length $(R/S)_\mu$ is deliberated. The rescaledrange approxes to: $(R/S)_\mu \approx c\mu^H$, in which $c$- invariable not dependent on $\mu$. Next, bring out the law of scaling using usual regression least squares on logs on both L.H.S. and R.H.S is applied to $\log(R/S)_\mu \approx \log c + H \log \mu$, in which $HE$ - Hurst exponent. Regression line slope in $(R/S)vs.t$ in log-log axes calculates

*Hurst exponent*. If $HE > 0.5$, the procedure involoves positive inappropriate for summing auto-covariance coefficients at all delays and is referred as continual. Whereas if $HE < 0.5$, the procedure involves negative and can be summed auto-covariances at all delays and is referred non-continual.
Consider $D = 2 - H$ where $1 \leq D \leq 2$ and is referred as the *Fractal Dimension*. The fractaldimension of a take statistical distribution denotes its self-similarity. It has been observed that the localized abnormality of series depends upon fractal dimensions. A value of 1.5 indicates Brownian motion.
*Index of Prediction* explains the activeness of time series i.e. $PI = 2|D - 1.5|$. If it is computed near zero, then the process approximates towards the chaotic orbit which is regarded as unpredictable. If it is computed around one, which categorizes the process as being predictable.

## 4 Results and Discussions

Using Equations (1-3), time series plot of each variable and statistical characteristics i.e. Slope, Mean, Standard Deviation, Kurtosis, Skewness, Hurst exponent, Fractal Dimension, Predictability Index are calculated. Also, log-log axes for $(R/S)$ vs time(t) were plotted to find the Hurst exponent. Fig.1,2 and 3 depict how each variable individually vary with time for variable $T, V, I$ respectively. Fig. 4, 5 and 6 shows log-log representation for $log(R/S)$vs.$log(time)$ for $T, V, I$ respectively. Table 1 and 2 gives the behaviour of statistical parameters with Hurst exponent, fractal dimesnsion of all variables.

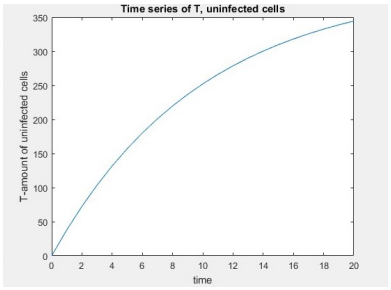


**Figure 1:** Time Series for Uninfected Cells, $T$

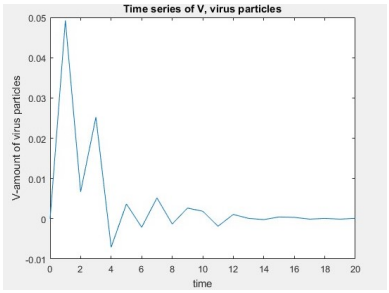


**Figure 2:** Time Series for Virus particles, $V$

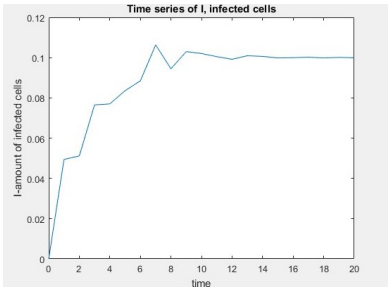


**Figure 3:** Time Series for Infected Cells, $I$

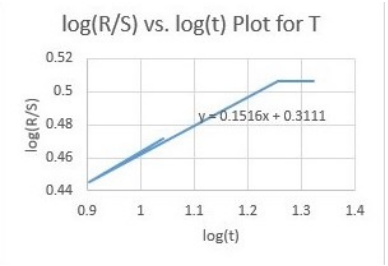


**Figure 4:** log(R/S)vs.log(time) of $T$

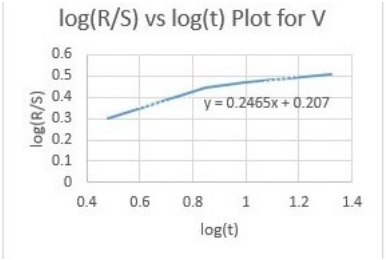


**Figure 5:** log(R/S)vs.log(time) of $V$

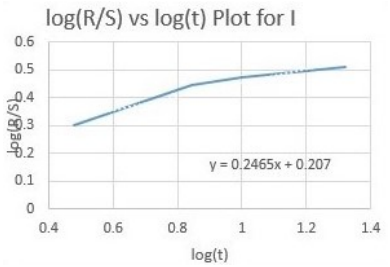


**Figure 6:** log(R/S)vs.log(time) of $I$

It is observed that the parameters $T, V$ and $I$ show anti-persistent behaviour. This implies that there will be a situation of chaos arising as the $HIV$ virion progresses inside the body cells.

**Table 1:** Statistical properties of the deterministic model variables

| Statistical Properties | $T(x_1)$ | $V(x_2)$ | $I(x_3)$ |
|---|---|---|---|
| Slope | 15.35733 | -0.00085 | 0.002947 |
| Mean | 223.6784 | 0.00399 | 0.087276 |
| Standard deviation | 104.774 | 0.011998 | 0.025613 |
| Skewness | -0.7601 | 3.181973 | -2.412 |
| Kurtosis | -0.50799 | 10.83628 | 6.273677 |

**Table 2:** Statistical properties of the deterministic model variables

| Statistical Properties | $T$-$t$ ($x_1$- $t$) | $V$- $t$ ($x_2$-t) | $I$-t ($x_3$-$t$) |
|---|---|---|---|
| Hurst Exponent | 0.15161 | 0.246452 | 0.246466 |
| Fractal Dimension | 1.84839 | 1.753548 | 1.753534 |
| Predictability Index | 0.69678 | 0.507096 | 0.507068 |
| Behaviour | Anti-persistence | Anti-persistence | Anti-persistence |

## Conclusion

It is observed from time series of $V$, virus particles in the blood grow exponentially in absence of any external factors whether environmental or treatment related. Simultaneously, $I$, amount of infected cells grows in the body causing a total failure of the immunity of the body system and $T$, amount of uninfected cells will decrease with time. Range of $V$, virus particles is very high as compared to $T$, uninfected and $I$, infected cells with time. $T$ and $I$ stabilize at a non-zero value after a period of time, there is an exponential increase in number of virus particles. The Hurst exponent, fractal dimension and index of prediction show anti-persistence behaviour of the variables with time. This implies that there will be a situation of chaos arising as the $HIV$ virion progresses inside the body cells. Thus, it has been observed that $HIV$ do not follow strictly deterministic model, it oscillates randomly which leads to deterministic equilibrium being not in fixed state at any instantenous time. Therefore, this Human Imnunodeficiency Virion system with ergodic disturbances help to alter the behaviour of dynamical system .

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## References

[1] J. Barunik and L. Kristoufek, On Hurst exponent estimation under heavy-tailed distributions, *Physica A*, **389** (2010), 3844-3855.

[2] J. Beard, F. Feeley and S. Rosen, Economic and quality of life outcomes of antiretroviral therapy for HIV/AIDS in developing countries: a systematic literature review, *AIDS Care*, **21** (2009), 1343-1356.

[3] R. Bhardwaj and A. Bangia, Complex Dynamics of Meditating Body, *Indian Journal of Industrial and Applied Mathematics*, **7** (2016),106-116.

[4] R. Bhardwaj, Wavelets and Fractal Methods with environmental applications, *Mathematical Models, Methods and Applications*. Eds:Siddiqi, A.H., Manchanda P., Bhardwaj R., (2016), 173-195.

[5] R. Bhardwaj, A. Kumar, P. Maini, S.C. Kar and L.S. Rathore, Bias free rainfall forecast and temperature trend based temperature forecast based upon $T$-170 Model during monsoon season. *Meteorological Applications*, **14** (2007), 351-360.

[6] C. Boshoff and R. Weiss, $AIDS$-related malignancies, *Nature Reviews Cancer* (2002), 373-382.

[7] G.E.P. Box, G.M. Jenkins, and G.C. Reinsel, *Time Series Analysis: Forecasting and Control*, Prentice Hall, 3rd edition, (1994).

[8] A. Carbone and G. Castelli, Noise in Complex Systems and Stochastic Dynamics, *Proceedings of SPIE* **5114**, 406 (2003).

[9] C. Chu and P.A. Selwyn, Complications of $HIV$ infection: a systems-based approach,*American family physician*, **83** (2011), 395-406.

[10] W.A. Fuller, *Introduction to Statistical Time Series*, Wiley Series in Probability and Statistics: Probability and Statistics, John Wiley and Sons, 2nd edition, (1996).

[11] D. Grech and Z. Mazur, Statistical properties of old and new techniques in detrended analysis of time series, *Acta Physica Polonica B* **36** (2005), 2403-2413.

[12] H. Hurst, Long term storage capacity of reservoirs, *Transactions of the American Society of Engineers*, **116** (1951), 770-799.

[13] M. Malta, S.A. Strathdee, M.M. Magnanini and F.I. Bastos, Adherence to antiretroviral therapy for human immunodeficiency virus/acquired immune deficiency syndrome among drug users: a systematic review, *Addiction* **103** (2008), 1242-1257.

[14] P.K. Nicholas, J.K. Kemppainen and G.E. Canaval, Symptom management and self-care for peripheral neuropathy in $HIV/AIDS$, *AIDS Care.***19**(2007), 179-189.

[15] A.S Perelson and P.W. Nelson, Mathematical analysis of $HIV-1$ dynamics in vivo, *SIAM Review* **41** (1999), 43-44.

[16] F. Post and S. Holt, Recent developments in $HIV$ and the kidney,*Current Opinion in Infectious Diseases* (2009), 43-48.

[17] G. Rangarajan and M. Ding, Integrated approach to the assessment of long range correlation in time series data, *Physical Review E.*, **61** (2000), 4991.

[18] G.P. Samanta, Permanence and extinction of a non-autonomous $HIV/AIDS$ epidemic model with distributed time delay, *Nonlinear Analysis: Real World Applications* **12** (2011), 1163-1177.

[19] B.D. Walker, Elite control of $HIV$ Infection: implications for vaccines and treatment,*Topics in HIV medicine: a publication of the International AIDS Society*, (2007), 134-136.

[20] X. Wanga, X. Liu, W. Xu and K. Zhang, Stochastic dynamics of $HIV$ models with switching parameters and pulse control, *Journal of Franklin Institute* **352** (2015), 2765-2782.

[21] R. Yarchoan, G. Tosato and R.F. Little, Therapy insight: $AIDS$-related malignancies - the influence of antiviral therapy on pathogenesis and management, *Nature Clinical Practice Oncology* (2005), 406-415.