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STOCHASTIC MODELLING OF SEVEN STAGES VIRAL LIFE CYCLE AND ESTIMATION OF VIRAL REPLICATION USING MODIFIED EXPONENTIAL POWER DISTRIBUTION-A BAYESIAN APPROACH

G. Meenakshi & S. Saranya

Department of Statistics, Annamalai University, Chidambaram, Tamil Nadu

ABSTRACT

Presently available viral dynamic research models are of the non-linear mixed effect models Most of the non-linear models developed by using the differential equations. Finding the solution of parameters are difficult if it is non-linear model. So, In this paper an attempt has been made to derived expected time of new viral budding consider kolmogrov in the life cycle of viral Dynamics. Predictive distribution of viral replication using modified Exponential power distribution through the Bayesian methodology has been derived.

KEYWORDS: *CD_4^+T Count, Exponential Power Distribution, Viral Load, Bayesian Approach*

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1. INTRODUCTION

At the end of 2011, globally, 34.0 million people were living with HIV. An estimated 0.8% of adults aged 15-49 year are living with HIV. The world Health organization (WHO) states clinical failure indicating severe immune deficiency among adults and adolescents. HIV produces millions of its copies in the bloodstream and consequently weakens the immune system by defeating WBCs. This type of WBC is called CD_4^+T cells or T-helper cells. HIV infected persons must go through antiretroviral treatment to fight infections. There is a way to treat HIV and no Vaccine is available yet, but HAART is an effective technique used to slow down the progression of the disease. The immunological failure as CD_4^+T count falls to the baseline (below 100 cell/mm^3) virology failure as plasma viral load measurements after 3 month with adherence support.CD_4^+T Count is best predictor for disease status and immediate risk of death and also used to identify those who have advanced HIV disease.There is no medicine to cure HIV infection is a challenge of physicians. So the researcher has developed statistical and mathematical modelling for the viral prediction. There are challenges in statistically modelling immune responses to longitudinal HIV viral load exposure as function of covariates. Bayesian Markov chain Monte Carlo mixed effect models to incorporate priors and examine different distributional assumptions. The improvement of health in HIV/AIDS patients on Highly Active Antiretroviral the reply is characterised by an increase in CD_4^+T counts and decrease in viral load to undetectable levels. In this research, seven stages of viral life cycle considered as continues time, discrete stage markov chain and modelling of viral replication in the Bayesian approach. In modelling HIV/AIDS progression in patients, researchers mostly deal with either viral load or CD_4^+T cell counts only. The orthogonal covariates viral load along with CD_4^+T baseline and using Bayesian methodology, viral prediction is determined.

2. REVIEW OF LITERATURE

Onoja Matthew Akpa (2010)studied the some of the models proposed by various authors for describing the epidemiology as well as the epidemiological consequences of the HIV/AIDS epidemic and how some of them could be modified to suit the situations in other countries. They also discussed the limitations and the place of such models in the fight against the HIV epidemic.R. Kannan and M. Iyappan (2017)have studied a stochastic model for estimating the expected time to seroconversion of HIV infected using preventive strategy. The effectiveness of the adoption preventive strategy in the elongation of the expected time to seroconversion by introducing the stochastic model under the assumption that the threshold level of antigenic diversity as a random variable which follows exponentiated modified Weibull distribution. G. Meenakshi, S. Lakshmi Priya (2018)have used the Bayesian Methodology is used to estimate the HIV replication for the future period per infected cell. In the HIV life cycle, there are seven different stages, such as binding, fusion, reverse transcription, integration, replication, assembly and budding. At the stage of binding, the various viral components bind with the cell. Such as a-Surface glycoprotein (gp120),b - trans membrane glycoprotein (gp41) CCR5, c - reverse transcriptase (P66 /P51) are considered to estimate the HIV replication. New risk function derived to use the components a, b and c. Finally, posterior parameter of HIV replication in a cell is estimated. The estimated parameter is compared with some standard parameter using various loss functions.G. Meenakshi and S. Saranya (2018) have derived a new modelled estimate the HIVreplication periodically using Markov processes in the condition of decay of CD_4^+Tcells. The proposed model is illustrated through numerically. Ali Raza, Muhammad Rafiq(2019) has explained a reliable numerical analysis of a stochastic HIV/AIDS model in a two-sex population considering counselling and antiretroviral therapy (ART). The authors are comparing the solutions of the stochastic and deterministic HIV/AIDS epidemic model. Xiaodan Sun, Hiroshi Nishiura(2019)has discussed Estimating HIV incidence is crucial for monitoring the epidemiology of this infection, planning screening and intervention campaigns, and evaluating the effectiveness of control measures. However, owing to the long and variable period from HIV infection to the development of AIDS and the introduction of highly active antiretroviral therapy, accurate incidence estimation remains a major challenge. Claris Shoko and Delson Chikobvu (2019) have studied CD_4^+T count and viral load as an essential component in monitoring HIV treatment outcome. However, CD_4^+T cell count monitoring sometimes fails to predict virological failure resulting in unnecessary switch of treatment lines which causes drug resistance and limitations of treatment options. Yan Wang, Tingting Zhao (2019) stochastic perturbation is introduced into HIV model with virus-to-cell infection, cell-to-cell transmission, CTLimmune response and three distributed delays. The stochastic integro-delay differential equation is transformed into degenerate stochastic differential equations. Examine that the influence of random fluctuations on model dynamics may be more significant than that of the delay. G. Meenakshi and P.R. Maheswari (2020)have derived the posterior distribution using the prior information in the Bayesian methodology. In the viral history, replication is increasing nature according to the time. So the viral replication is considered as Rayleigh random variable. The predictive distribution obtained and finding the expected number of viral replication is illustrated through the graph. Steven G. Deekset al (2021) have developed the success of antiretroviral therapy (ART) for people living with HIV, lifelong treatment is required and there is no cure. HIV can integrate in the host genome and persist for the life span of the infected cell. G. Meenakshi and P.R. Maheswari (2021)have derived the posterior distribution of Weibull distribution by using various priors and estimate the Bayes risk. Simona Claudia Cambrea (2022) have modelled Comparing different variables of HIV-positive pregnant women from the two HIV-AIDS CRs, there are significant differences between the mean value of hemoglobin, CD_4^+ level, environmental area, marital and amniotic membranes status, and HIV patient stage in the last trimester of pregnancy ($p < 0.05$), but without any differences in

mother's mean age, education level, type of delivery, breastfeeding, the duration of cART administration, HIV viral load, and survival rate. In this research the seven stage of viral life cycle is considered as the markov differential equation and viral replication is estimated by Bayesian methodology.

3. STOCHASTIC MODEL FOR SEVEN STATES IN THE VIRAL LIFE CYCLE

1. Binding

During the first Stage of HIV life cycle, the virus binds to receptors on the surface of CD_4^+T cells. CD_4^+TCells, also call helper T cells, are a type of White blood cell that alerts immune cells that there is an infection in our body.

2. Fusion

HIV is an enveloped virus, meaning that its genetic information is protected by both a protein shell and a lipid layer called an envelope.Once HIV binds to receptors on CD_4^+T cells, it initiates the fusion of its envelope with the membrane of the CD_4^+Tcell using a glycoprotein called GP120 Trusted Source. Glycoproteins are molecules made of chains of carbohydrates and proteins. Fusing with the membrane of your CD_4^+T cells allows the virus to enter the cell.

3. Reverse transcription

Reverse transcription is a process of converting genetic information in the form of RNA into DNA. RNA and DNA contain similar genetic information but are structurally different. RNA is typically made up of one long chain of genetic information, while DNA is made up of a double strand. The virus converts its RNA into DNA by releasing an enzyme called reverse transcriptase. This process allows the virus' genetic information to enter the nucleus ofCD_4^+T cell

4. Integration

Once HIV has converted its RNA into DNA, it then releases another enzyme called integrase inside the nucleus ofCD_4^+T cell. The virus uses this enzyme to combine its DNA into the DNA ofCD_4^+T cell.At this point, the infection is still considered latent and is difficult to detect even with sensitive laboratory tests.

5. Replication

Because HIV is now integrated intoCD_4^+T cell's DNA, it can use that cell's machinery to generate viral proteins. During this time, it can also produce more of its genetic material (RNA). These two things allow it to create more viral particles.

6. Assembly

In the assembly stage, new HIV proteins and RNA are sent to the edge of CD_4^+T cell and become immature HIV. These viruses are non-infectious in their current form.

7. Budding

During the budding stage, the immature viruses push out ofCD_4^+T cell and then release an enzyme called protease that modifies proteins in the virus and creates a mature and infectious virus.

In the viral dynamic study, the maturity of the viral replication during the seven stages, namely (1) Binding (2) fusion (3) reverse transcription (4) integration (5) transcription (6) translation (7) viral assembly and maturation. Those seven stages are considered as continuous time, discrete state Markov chain as follows,

t_{ij} denote the time duration between the i[th] stages to j[th] stage $i = 1,2,\dots,7, j = 2,\dots,7$.

$$t_{12} > t_{23} > t_{34} > t_{45} > t_{56} > t_{67}$$

Let $P_{ij}(t_{ij})$ denote the probability in the i^{th} stage (state) to the (j^{th} state) at the time duration t_{ij}. The probability is decreasing nature for every succeeding state $P_{ij} > 0$.

Where

$$P_{12} > P_{23} > P_{34} > P_{45} > P_{56} > P_{67}, P_{ij} > 0$$

The Expected time required per new virus maturation is denoted by $E(T) = \sum_{ij} t_{ij} P_{ij}, \quad P_{ij} > 0, and t_{ij} > 0, \ i \neq j$ The seven stage (state) transition probabilities are as follows

$$P_1 = P_{12}$$

$$P_2 = P_{12} \cdot P_{23}$$

$$P_3 = P_{12} \cdot P_{23} \cdot P_{34}$$

$$P_4 = P_{12} \cdot P_{23} \cdot P_{34} \cdot P_{45}$$

$$P_5 = P_{12} \cdot P_{23} \cdot P_{34} \cdot P_{45} \cdot P_{56}$$

$$P_6 = P_{12} \cdot P_{23} \cdot P_{34} \cdot P_{45} \cdot P_{56} \cdot P_{67}$$

Where

$$P_1 > P_2 > P_3 > P_4 > P_5 > P_6, P_{ij} \neq P_{ij+1}$$

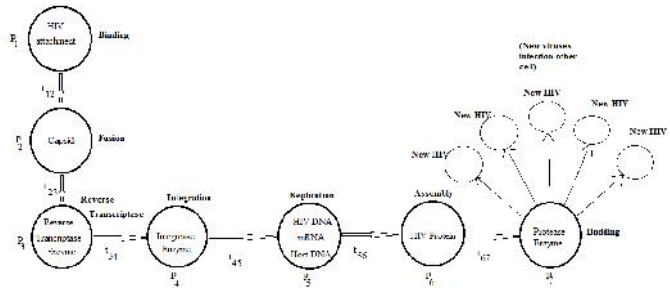


Figure 1.

The seven state transition probability matrix for nCD_4^+T cell is given by

$$CD_4^+ cell \begin{matrix} \\ 1 \\ 2 \\ 3 \\ \vdots \\ n \end{matrix} \begin{matrix} states \\ 1 \quad 2 \quad 3 \quad 4 \quad 5 \quad 6 \quad 7 \end{matrix} \begin{bmatrix} P_{11} & P_{12} & P_{13} & P_{14} & P_{15} & P_{16} & P_{17} \\ P_{21} & P_{22} & P_{23} & P_{24} & P_{25} & P_{26} & P_{27} \\ P_{31} & P_{32} & P_{33} & P_{34} & P_{35} & P_{36} & P_{37} \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ P_{n1} & P_{n2} & P_{n3} & P_{n4} & P_{n5} & P_{n6} & P_{n7} \end{bmatrix}$$

In the viral lifecycle, the Expected time of new virus budding becomes the modified Kolmogorov differential equation it is denoted by

$$P_{i,0}(t_{ij}) = \sum_{\substack{i=1 \\ s=1}}^{7} P_{i,s}(t_i) \times P_{s,0}(t_6)$$

is the probability that i^{th} state will be in the 0^{th} state at time $t_{12} + t_{23} + t_{34} + t_{45} + t_{56} + t_{67} = t$, where t_{ij} are the continuous time interval will be decreasing nature of succeeding periods it is given by

$$P_{i0}(t) = P((X = t) = o/X(t_{01}) = i, X(t_{12}) = j, X(t_{23}) = k, X(t_{34}) = l, X(t_{56}) = m, X(t_{67}) = n)$$

This model follows the modified linear growth process with immigration growth rate (when immigration growth rate is the dependent to one stage to another stage. Where t_{ij} the intervals are not equal. But deceasing random variable with interval

$$[a_i, a_j], i = 0,1,2, \dots,7, j = 1,2, \dots,7.$$

$$[a_0, a_1] \neq [a_1, a_2] \neq [a_2, a_3] \neq [a_3, a_4] \neq [a_4, a_5] \neq [a_5, a_6] \neq [a_6, a_7]$$

$[a_0, a_1] > [a_1, a_2] > [a_2, a_3] > [a_3, a_4] > [a_4, a_5] > [a_5, a_6] > [a_6, a_7]$ then its density function is denoted by,

$$f(t_i) = \frac{2e^t}{\alpha(1+e^{-t})}, \qquad \alpha_i > 0, \alpha_1 > \alpha_2 > \cdots > \alpha_7.$$

α_i −is theevery stage varying ratio (RNA concentration) Expected time to maturation of viralreplication. It is given by

$$E(T) = \int_{a_1}^{a_7} t \cdot f(t) \cdot dt$$

$$E(T) = \int_{a_1}^{a_7} \frac{t\, 2e^t}{\alpha(1+e^t)} dt$$

$$= \int_{a_1}^{a_7} \frac{t\, 2e^t}{\alpha(1+e^t)} dt$$

$= \frac{2}{\alpha} \int_{a_1}^{a_7} \frac{t.e^t}{(1+e^t)} dt \text{Letz} = 1 + e^t$

$$= \frac{2}{\alpha} \int_{a_1}^{a_7} \frac{logz}{z} dz \; logz = t$$

$$= \frac{2}{\alpha} \left[\frac{logz}{2}\right]^2 dz = e^t dt$$

$$E(T) = \frac{1}{\alpha} (logz)^2$$

$$= \frac{1}{\alpha} [\log(1+e^t)]$$

$$E(T^2) = \int_{a_1}^{a_7} \frac{2t^2.e^t}{\alpha(1+e^t)} dt$$

$= \frac{2}{\alpha}\int_{a_1}^{a_7} \frac{t^2.e^t}{(1+e^t)}$ let $z = 1 + e^t$

$$= \frac{2}{\alpha}\int_{a_1}^{a_7} \frac{2logz}{2}\, dz 2logz = t^2$$

$$= \frac{4}{\alpha}\int_{a_1}^{a_7} \frac{logz}{2}\, dzdz = e^t dt$$

$$= \frac{4}{\alpha}\left[\frac{(logz)^2}{2}\right]$$

$$= \frac{2}{\alpha}[(logz)^2]_{a_1}^{a_7}$$

$$= \frac{2}{\alpha}(logz)^2$$

$$= \frac{2}{\alpha}[\log(1+e^t)]^2$$

$$V(T) = E(T^2) - (E(T))^2$$

$$= \frac{2}{\alpha}(logz)^2 - \left[\frac{(logz)^2}{\alpha}\right]^2$$

$$= \frac{4}{\alpha}logz - \frac{4logz}{\alpha^2}$$

$$V(T) = \frac{4}{\alpha}\log(1+e^t) - \frac{4}{\alpha^2}\log(1+e^t)$$

4. BAYESIAN MODEL FOR VIRAL REPLICATION

Viral replication in the CD_4^+T cells of Biological system is similar but it is the reverse order to the chemical reactor Experiment. Developing viral replication model using the new modified Exponential power distribution. In the chemical reactor experiment outlet concentration is smaller than the input concentration. But viral replication system, outlet concentration is greater than the inlet viral concentration. In the new virus maturation, there are seven stages. The average viral replication $E(y) = \eta(\theta_i/\xi)$ is the non-linear function.

Where,

$$E(y) = \eta(\theta_i/\xi)$$

$$y = \eta(\theta_i/\xi) + e_i$$

$$\eta(\theta_i/\xi) = \theta_i\xi$$

y- is the outlet viral replication per CD_4^+T cells after infection.

ξ- is the inlet viral fixed viral RNA to the CD_4^+T cells.

θ- is average replication for 7th stage,

$$\theta = f(\theta_1, \theta_2, \dots, \theta_7, x_1, x_2, \dots x_7).$$

$$= \theta_1 x_1 + \theta_2 x_2 + \cdots + \theta_7 x_7 + \xi, i = 1,2, \dots, 7$$

Where,

$x_i - i^{th}$ stage CD_4^+T cell DNA and enzymes concentration

θ_i - i^{th} stage viral RNA Concentration,

$$x_i = 2x_{i-1}, i = 1,2, \dots, 7 \text{ and } x_1 = 2x_0, \qquad x_0 = 1$$

i^{th} Stage CD_4^+T cell concentration is depends on the provirus stage concentration

θ_i and x_i are the random variable with parameter θ, σ, β

y -Outlet viral replication.

σ- is the scale parameter in each stage variation of enzymes concentration.

β- is the nuisance parameter, $0 < \beta \leq 1$ possitively correlation between CD_4^+T cells

DNA Concentration and viral RNA concentration for all the seven stages.

At the time of infection, viral RNA concentration in the CD_4^+T as unity. At the next stage concentration may be similar to the chemical reactor experiment but it results are in the reverse order. In the chemical reactor experiment, outlet concentration is random variable with its range is $-\infty < y < \infty$. At the time of outlet, the concentration is reduced in the chemical reactor Experiment the ever follows the exponential power distribution is used by Diananda (1949), Box (1953b) and Turner (1960). They assumed that input concentration is fixed and outlet concentration is random variable.

In this research, the final stage viral concentration is increasing nature. It is follow the modified exponential power distribution with range $0 < y < \infty$ with parameter θ, σ, β.

$$y - E(y) = e$$

The likelihood function is given by

$$l(\theta, \sigma, \beta / y) \propto {}^1/_2 \omega(\beta) e^{-n} exp\left\{-C(\beta) \sum \left|\frac{e_i}{\sigma}\right|^{2(\beta+1)}\right\}$$

Where,

$$e_i = y_i - E(y_i), \qquad 0 < \beta \leq 1, \qquad 0 < y < \infty, \quad \sigma > 0.$$

$$C(\beta) = {}^1/_2 \left\{\frac{[\Gamma\, {}^3/_2 (1+\beta)]}{[\Gamma\, {}^1/_2 (1+\beta)]}\right\}^{{}^1/_{1+\beta}}$$

$$\omega(\beta) = {}^{1}/_{2}\frac{\left[\Gamma\,{}^{3}/_{2}\,(1+\beta)\right]^{1/2}}{(1+\beta)\left\{\Gamma\,{}^{1}/_{2}\,(1+\beta)\right\}^{3/2}}$$

The non-informative the prior distribution of σ is given by $P(\sigma) = {}^{1}/_{\sigma}$.

The posterior distribution of θ given σ, β is propositional to

$$P(\theta/\sigma,\beta,y)\alpha\, l(y/\theta,\sigma,\beta)p(\sigma)$$

$$\alpha\ \sigma^{-n}\ exp^{-c(\beta)}\sum\left|\frac{e_i}{\sigma}\right|^{2(\beta+1)}\frac{1}{\sigma}$$

$$\alpha\ \frac{1}{\sigma^{(n+1)}}e^{-c(\beta)}\sum_{i=1}^{n}\left(\frac{e_i}{\sigma}\right)^{2(1+\beta)} \qquad 0 \le \beta \le 1,\ \ \sigma > 0,$$

The Prior distribution of β is uniform distribution

$$P(\beta/y) \simeq 1 \qquad 0 < \beta \le 1$$

The marginal density of the θ is integrated out $\left({}^{1}/_{\sigma}\right)$

The posterior density is given by.

$$P(\theta/\beta,y)\ \alpha\ \int_0^{\infty}\frac{1}{\sigma^{n+1}}e^{-c(\beta)}\sum_{i=1}^{n}\left(\frac{e_i}{\sigma}\right)^{2(1+\beta)}d\left({}^{1}/_{\sigma}\right).$$

Let $\left({}^{1}/_{\sigma}\right) = x$

$$\alpha\ \int_0^{\infty}x^{(n+1)}e^{-c(\beta)}\sum_{i=1}^{n}(e_i x)^{2(1+\beta)}\,dx.$$

The marginal distribution becomes the weibull distribution.

$$P(\theta/\beta,y)\alpha\int_0^{\infty}x^{n+2-1}\,e^{-c(\beta)^n(\sum x)^c}dx.$$

Where $a = c(\beta)(\sum e_i)^c, b = n+2, c = 2(1+\beta)$.

The normalizing constant

$$\int_0^{\infty}x^{(n+2)-1}\,e^{-c(\beta)e(nx)^c}dx.$$

$$= \frac{1}{ab}$$

$$= \frac{1}{c(\beta)(\sum e_i)^c.(n+2)}$$

$$= \frac{1}{c(\beta)(\sum y_i - \eta(\theta/\xi)).2(1+\beta)(n+2)}$$

$$P(\theta/\beta, y) = \frac{(1/\sigma)^{n+2-1} e^{-c(\beta)\sum y_i - \eta(\theta/\xi)(1/\sigma)^{2(1+\beta)}}}{n(n+2)c(\beta)(y_i - \eta(\theta/\xi))}$$

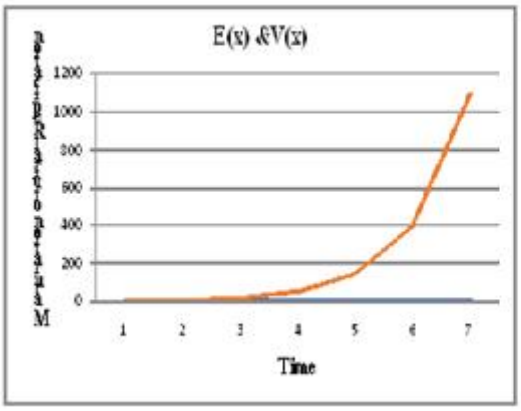
Mean of the distribution is given by

$$E(X) = C(\beta)\left(\sum(y_i - \eta(\theta/\xi))\right)^{-(1/n+2)} \Gamma(1 + 1/n+2)$$

6. Numerical Result

Table 1: Maturation of Viral Replication for Different Time Periods Mean and Variance

Time	Mean	Variance
1	1.1406	1.5775
2	1.8474	5.5416
3	2.6479	17.4375
4	3.4901	51.1080
5	4.3487	144.064
6	5.2136	398.21
7	6.0809	1090.5



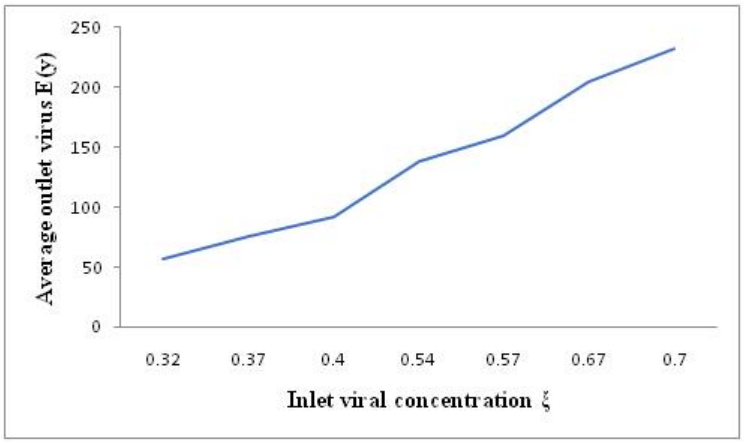
Graph 1: Maturation of Viral Replication Various Scale Parameters Mean and Variance

Graph – I that Maturation of viral replication is mean and variance increases. Whenever the time increase.

Table 2: Viral Replication for different Time Periods. Variance Versus Scale Parameter of the Exponential Power Distribution,

x^t	ξ^1	ξ^2	ξ^3	ξ^4	ξ^5	ξ^6	ξ^7
1	0.3	0.5	0.8	1	1.2	1.4	1.6
2	0.5	0.8	1	1.2	1.4	1.6	1.8
4	0.8	1	1.2	1.4	1.6	1.8	2
8	1	1.2	1.4	1.6	1.8	2	2.2
16	1.2	1.4	1.6	1.8	2	2.2	2.4
32	1.4	1.6	1.8	2	2.2	2.4	2.6
64	1.6	1.8	2	2.2	2.4	2.6	2.8
E(y)	**57.12**	**75.66**	**92**	**137.91**	**160.05**	**205.15**	**232.12**

Inlet Viral concentration(ξ_i)	0.32	0.37	0.4	0.54	0.57	0.67	0.7
Average Outlet virus E(y)	57.12	75.66	92	137.91	160.05	205.15	232.12



Graph 2: Viral Loads Various Scale Parameter of Exponential Power Distribution.

The viral RNA Concentration increases, the Average viral replication of outlet also increases.

Table 3: Viral Replication for Different Time Periods The Various Shape Parameter of the Exponential Power Distribution, $\theta_{ii} = 1, 2, \ldots, 7$ (Square Of x_i)

x^i	$\xi^1 = 0.32$ θ_{1i} 0.3	$\xi^2 = 0.37$ θ_{2i} 0.5	$\xi^3 = 0.4$ θ_{3i} 0.8	$\xi^4 = 0.54$ θ_{4i} 1	$\xi^5 = 0.57$ θ_{5i} 1.2	$\xi^6 = 0.67$ θ_{6i} 1.4	$\xi^7 = 0.7$ θ_{7i} 1.6
1	0.3	0.5	0.8	1	1.2	1.4	1.6
3	0.5	0.8	1	1.2	1.4	1.6	1.8
9	0.8	1	1.2	1.4	1.6	1.8	2
81	1	1.2	1.4	1.6	1.8	2	2.2
6561	1.2	1.4	1.6	1.8	2	2.2	2.4
43,046,	1.4	1.6	1.8	2	2.2	2.4	2.6
721	1.6	1.8	2	2.2	2.4	2.6	2.8
1.85302 019E+1 5							

Inlet Viral Concentration(ξ_i)	**Average Outlet Virus E(y)**
0.32	2.96483236E+15
0.37	3.33543641E+15
0.4	4.07664450E+15
0.54	5.87357250E+15
0.57	6.44612046E+15
0.67	7.56264105E+15
0.7	8.29543964E+15

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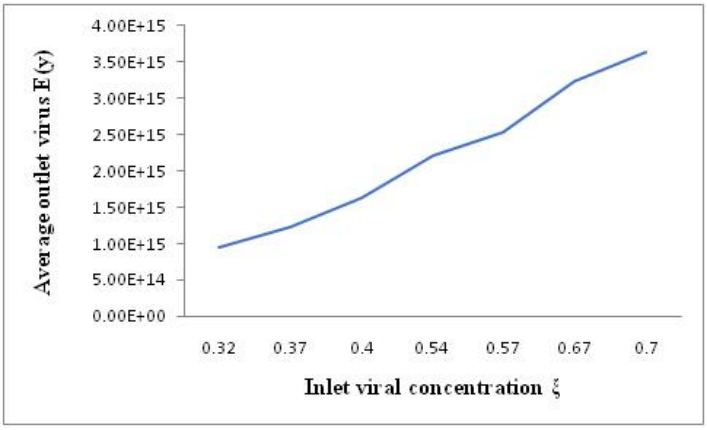


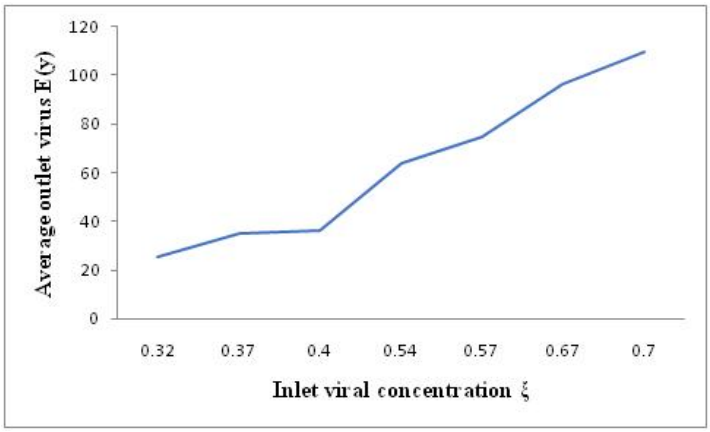
Graph 3: Viral Loads Various Scale Parameter of Exponential Power Distribution.

The inlet viral concentration in terms of square of x_i increase.The outlet viral concentration also increases, of the some period as compare to the previous table.

Table 4: Viral Replication for Different Time Periods. [illegible] Various [illegible] Parameter of the Exponential Power Distribution, [illegible]

x^i	0.32	0.37	0.4	0.54	0.57	0.67	0.7
	$\xi_1 = \theta_{1i}$ 0.3	$\xi_2 = \theta_{2i}$ 0.5	$\xi_3 = \theta_{3i}$ 0.8	$\xi_4 = \theta_{4i}$ 1	$\xi_5 = \theta_{5i}$ 1.2	$\xi_6 = \theta_{6i}$ 1.4	$\xi_7 = \theta_{7i}$ 1.6
1	0.3	0.5	0.8	1	1.2	1.4	1.6
3	0.5	0.8	1	1.2	1.4	1.6	1.8
6	0.8	1	1.2	1.4	1.6	1.8	2
9	1	1.2	1.4	1.6	1.8	2	2.2
12	1.2	1.4	1.6	1.8	2	2.2	2.4
15	1.4	1.6	1.8	2	2.2	2.4	2.6
18	1.6	1.8	2	2.2	2.4	2.6	2.8
E(y)	**25.53**	**35.26**	**36.32**	**64.04**	**74.89**	**96.61**	**109.61**

ξ_i	0.32	0.37	0.4	0.54	0.57	0.67	0.7
E(y)	25.53	35.26	36.32	64.04	74.89	96.61	109.61

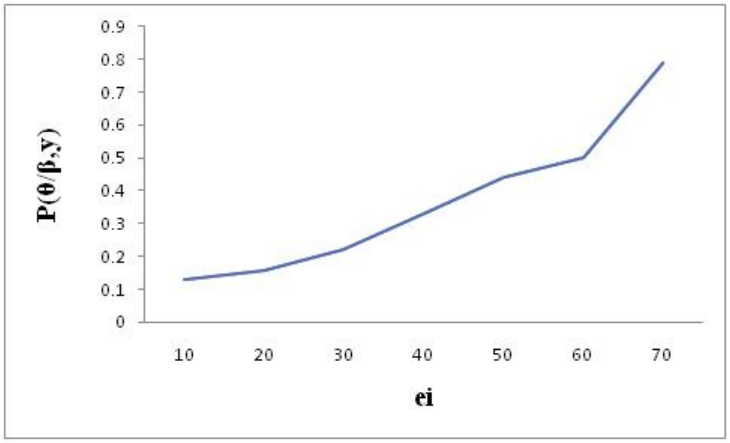


Graph 4: Viral Loads Various Scale Parameter of Exponential Power Distribution.

The inlet viral concentration increase, the outlet viral concentration (replication) also increasesafter some period.

Table 5: Posterior Density of Viral Load From the Viral Replication For Different Time Periods with Special Case of the Viral = β 0.25, σ^2 The Scale Parameter of the Exponential Power Distribution

	P(/)
10	0.129
20	0.155
30	0.220
40	0.329
50	0.44
60	0.503
70	0.791

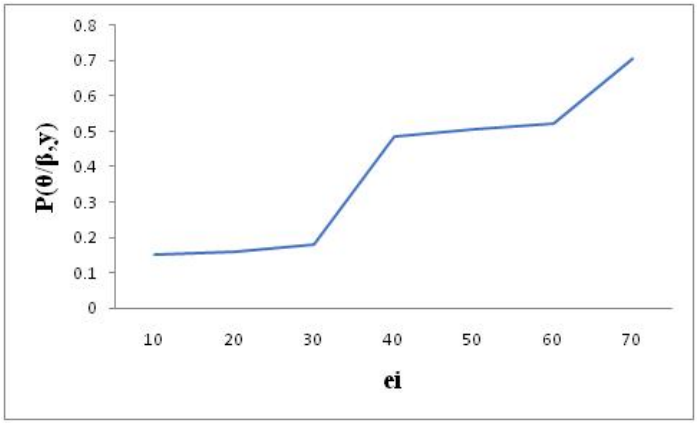


Graph 5: Posterior Density of Viral Loads Using Various Scale Parameter of Exponential Power Distribution.

The gradually increases the posterior density of viral replication.

Table 6: Posterior Density Viral Load for the Viral Replication for Different Time Periods with Special case of Viral = β 0.5, σ^2 the Scale Parameter of the Exponential Power Distribution

	P(/)
10	0.150
20	0.158
30	0.178
40	0.486
50	0.507
60	0.524
70	0.706

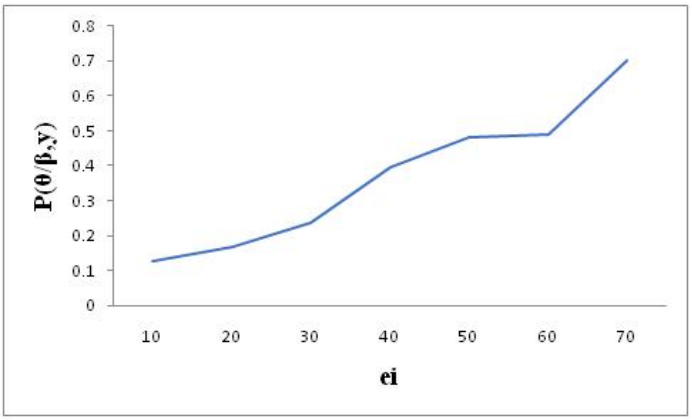


Graph 6: Posterior Density of Viral Loads Using Various Scale Parameter of Exponential Power Distribution.

The gradually increases the posterior density of viral replication.

Table 7: Posterior Density for the Viral Replication for Different Time Periods with Special Cases = Viral Load The Scale Parameter of the Exponential Power Distribution

[illegible]	P([illegible]/[illegible])
10	0.129
20	0.169
30	0.237
40	0.395
50	0.480
60	0.490
70	0.701

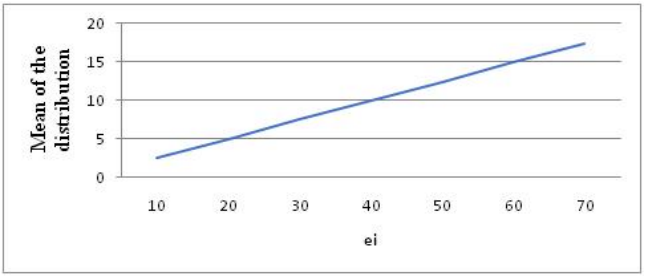


Graph 7: Posterior Density Viral Loads Various Scale Parameter of Exponential Power Distribution.

The gradually increases the posterior density of viral replication.

Table 8: Mean of the Distribution of Viral Replication For Different Time Periods with Special Case N=7

	Mean of the Distribution
1	2.47
2	4.94
3	7.41
4	9.88
5	12.35
6	14.82
7	17.29



Graph 8: Viral Replication for Various Scale Parameters.

The error term of the distribution is increase. Average viral distribution positively correlated.

7. CONCLUSION

In this research, the seven stage of viral replication are modelled as kolmogrov differential equation and the average viral replication is considered as non-linear function. Then the posterior distribution of seven stages using Exponential Power Distribution and obtained the average distribution of viral replication for the future period through the posterior distribution. It is very much useful for the treatment to the HIV infected person.

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