

Stochastic Modeling of the Mechanism in Virus Growth of Cells in HIV Infected Person

S. Saranya, G. Meenakshi

Abstract: *The overall time required for a virus to reproduce depends collectively on the rates of multiple stages in the infection process, including initial binding of the virus particle to the surface of the cells, virus internalization and release of the virus genome, association of descendent virus particles, and release of these particles into the extracellular atmosphere. For a large number of virus type, much has been learned about the molecular, RNA or protein expression genome replication rates of the various stage. However, an attempt is been made using stochastic modeling to the overall timing and productivity of the infection stage in a cell. The numerical result to predict the probability of infection given the communication of the virus to a new individual.*

Keywords : *Branching Process, Poisson Property, Exponential Logarithmic Application and Normal Distribution.*

I. INTRODUCTION

A noteworthy test in science is to anticipate how life forms will carry on dependent on how they communicate with their surroundings. This is hard in light of the fact that basic practices, for example, how life forms imitate or create, rely upon detecting and reacting to assorted ecological variables, regularly including the initiation and articulation of numerous qualities just as composed connection among different quality items. To address this test, it might begin little by focusing on the least complex living beings, whose development and advancement are encoded by the most limited genomes, including a sensible number of fundamental qualities and co operations. Concentrates on infections that contaminate microbes, the bacteriophages, assumed a key job in original revelations of atomic science. For instance, early investigations on phage CD₄⁺ T cell by Hershey and Chase gave convincing proof of the job of nucleic acids, not proteins, as the material that encodes hereditary data. Each genome in nature encodes various procedures, and genomes of infections are no special case. In a suitable domain of a living cell, the arrival of a genome from an attacking infection can take order, coordinating material and vitality assets from cell forms and toward the combination of parts that are basic for infection development, i.e., viral mRNA, viral proteins, viral genomes, and lipids of viral layers. Gathering of these and different parts produces descendant's infection particles that, upon discharge by the phone, may then contaminate other defenseless cells. For some infections, including infections that taint organisms,

Revised Manuscript Received on October 01, 2019.

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plants, creatures, and people, fundamental sub-atomic procedures of intracellular improvement have been explained. In any case, in spite of the moderately short lengths of infection genomes, the systems of responses that characterize infection development and their collaborations with their host cells stay complex. These systems can contain numerous positive and negative criticisms that make it trying to foresee how bothers to viral or have cell capacities, either by hereditary designing or by the nearness of medications that explicitly target viral or cell capacities, will quantitatively impact infection creation or cell endurance.

II. REVIEW OF LITERATURE

Andrei Y. Yakovlev, (2018) have discussed first approach, known as clonal analysis, is designed to make indirect inferences of cell cycle parameters from cell counts.

Abid Ali Lashari1 · Pieter Trapman1, (2017) have explained in our model we assume that individuals enter the population at rate μN (i.e. according to a Poisson process with intensity μN) and that individuals have independent exponentially distributed "lifetimes" (or time they stay in the active population), with expectation $1/\mu$, i.e. individuals leave the active population at rate μ times the number of individuals in this population.

Ruy M. Ribeiro, (2010) have studied Estimating R from equation requires having enough data to estimate all seven parameters in this equation. Who analyzed data collected over the first 80 to 100 days of infection, used this approach.

D. Dolgopyat, (2018) have briefly the current paper concerns the long-time behavior of multi-type branching processes with time-dependent branching rates.

E.O. Romero-Severson, (2014) have explained this problem by deriving probability generating functions to express the probability that a newly infected individual generates a given number of infections, a random variable that we refer to as H^* . Generating functions have been successfully applied to a wide variety of infectious disease epidemiology problems.

Scott P. Layne, Micah Dembo, and John L. Spouge(1989) have consideration a number of kinetic processes occur simultaneously. Infection of target cells occurs in multiple stages: first, a virus diffuses to the cell surface; second, the $gp120$ glycoproteins on the virus's surface and CD4 on the target cell's surface form bimolecular complexes; and third, interactions involving CD4, $gp120$, and $gp41$ (which is attached to $gp120$) promote fusion of the HIV envelope with the target-cell membrane, resulting in entry of the viral core into the cell.

G. Meenakshi and S. Saranya, (2018) have discussed this paper concentrated to the periodically viral replication of infected persons. The stochastic models are designed for the viral replication in the CD₄⁺ T cells and lysing CD₄⁺ T cells count and illustrated.

T. E. Harris, have illustrated refer the consider an initial object (ancestor) forming the zero generation. This object has probabilities P_r, r = 0,1,2, of producing r objects, which will constitute the first generation.

Giuseppe Di Biase, Guglielmo D'Amico, (2007) have explained the acquired immunodeficiency syndrome (AIDS) is caused by the human immunodeficiency virus (HIV), a virus belonging to the lentivirus subgroup of retroviruses.

III. MODELS

A. Stochastic branching process:

Stochastic branching processes are analytically treated by the use of the probability generation function.

$$G(s) = \sum_{r=0}^{\infty} p(r) s^r$$

Introduce the Poisson property,

It x (t) denotes number of (actual) viral load includes (0, t) & follows Poisson process with parameter λ.

The viral load include nth time independently with probability P. N (t) denotes number of nth time in (0, t) then N (t) is also a Poisson process with parameter λP.

Suppose 'n' particles are time then actual viral load include may be n + r where r = 0,1,2,3, ...
So

$$p[N(t) = n] = \sum_{r=0}^{\infty} p[x(t) = n + r] \& \frac{n^{th} \text{ time}}{n + r \text{ viral load}}$$

Viral load and nth time are independents

$$\begin{aligned} &= \sum_{r=0}^{\infty} p[x(t) = n + r] \cdot p[n^{th} \text{ time of } n + r \text{ viral load}] \\ &= \sum_{r=0}^{\infty} \frac{e^{-\lambda} (\lambda)^{n+r}}{(n+r)!} \cdot (n+r) c_n p^n q^{n+r-n} \\ &= e^{-\lambda} (\lambda)^n p^n \sum_{r=0}^{\infty} \frac{(\lambda)^r}{(n+r)! n! (n+r-n)!} q^r \\ &= e^{-\lambda} (\lambda)^n \sum_{r=0}^{\infty} \frac{(\lambda q)^r}{n! r!} \\ &\therefore \left[1 + \frac{x}{1!} + \frac{x^2}{2!} + \frac{x^3}{3!} + \dots + e^x \right] \\ &\frac{e^{-\lambda} (\lambda p)^n}{n!} \left[1 + \frac{\lambda q}{1!} + \frac{(\lambda q)^2}{2!} + \dots \right] \\ &= \frac{e^{-\lambda} (\lambda p)^n}{n!} e^{\lambda q} \\ &= \frac{e^{-\lambda(1-q)} (\lambda)^n}{n!} \\ &= \frac{e^{-\lambda p} (\lambda p)^n}{n!} \end{aligned}$$

If n itself is a random variable then the sum of random variable

S=X₁ + X₂ + ... + X_n is generate by

$$G(s) = \frac{e^{-\lambda p} (\lambda p)^n}{n!}$$

$$\begin{aligned} X \sim \text{poisson process (k)} \quad G(s) &= \frac{e^{-\lambda p} (\lambda p)^n}{n!} \\ &= G(s_1) \\ &= G(G(s_2)) \\ &= G(G(G(s_2))) \\ &\dots \\ &= G(s_n) \end{aligned}$$

B. Multiscale Modeling of Virus Infection Spread

Virus infections of host cells amplify over multiple generations, requiring the intracellular processes that are the focus of this review to play out over multiple cycles of susceptible host cell infection. The viral progeny released from an initial infected host cell go on to further infect other host cells, perhaps in the same tissue of a multicellular host organism.

C. Multi type Branching Process

Now suppose that we can distinguish r type of individual, type 1,2, ... k. Each individual has a unit life-length, and if it is of type k, then it splits into k₁ offspring of types 1 k₂ offspring of type 2, ..., up to k_r offspring of type with probability p_k(k₁, k₂, ..., k_r).

Population of individual originates with a single ancestor and that there are k (finite) type of individuals. Let p⁽ⁱ⁾(r₁, r₂, ... r_k) be the probability that an individual of type i produces r_j offspring of type j, j = 1,2,3, ..., k.

Let f⁽ⁱ⁾(s) = ∑ p⁽ⁱ⁾ s^{r₁} s^{r₂} ... s^{r_k} be the probability generation function of {p⁽ⁱ⁾(r)}. Let X_n = X_n¹, X_n², ..., X_n^k represent the population size of k types in the nth generation. Let m_{ij} be the expected number of offspring of type j produced by an object of type i,

$$\begin{aligned} f_n^{(i)}(s) &= f^{(i)}(f_{n-1}^{(1)}(s), f_{n-1}^{(2)}(s), \dots, f_{n-1}^{(n)}(s)) \\ f_0^{(i)}(s) &= s_i, i = 1,2, \dots, k; n = 0,1,2, \dots \end{aligned}$$

The population becomes extinct when x_n = 0 for some n ≥ 1.

$$\begin{aligned} q_n^{(i)} &= pr\{X_n = 0 / X_0 = e_i\} \\ q_n^{(i)} &= \lim_{n \rightarrow \infty} q_n^{(i)} \end{aligned}$$

D. The mean matrix:

Let z_{1,j}⁽ⁱ⁾ be the number of type j offspring of a single type i particle in one generation.

We assume that

$$0 < m_{ij} = \sum z_{1,j}^{(i)} < \infty$$

and we define the mean matrix

$$M = (m_{i,j})_{i,j=1,2,\dots,r}$$

Let z_n = (z_{n,1}, ..., z_{n,r}), or when the process start with one particle in state i. We denote it by z_n⁽ⁱ⁾, then

$$E[z_n / z_0] = z_0 M^n.$$

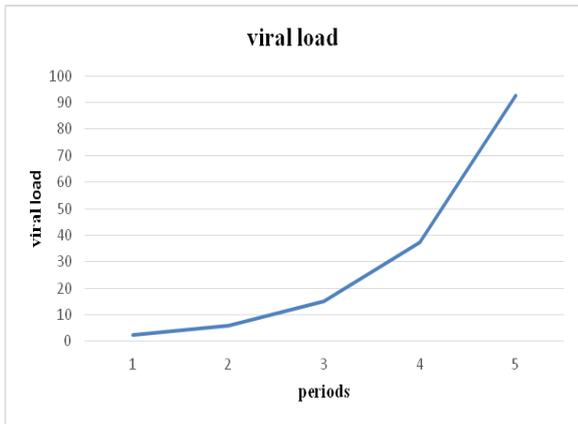


Numerical Results

From eqn (1), the below table1 illustrates the viral load for different time periods with special case $\lambda = 2, P = 1, n = 5$.

| Time period | Viral load |
|-------------|------------|
| 1 | 2.4741 |
| 2 | 6.1212 |
| 3 | 15.1445 |
| 4 | 37.4690 |
| 5 | 92.7021 |

GRAPH: I

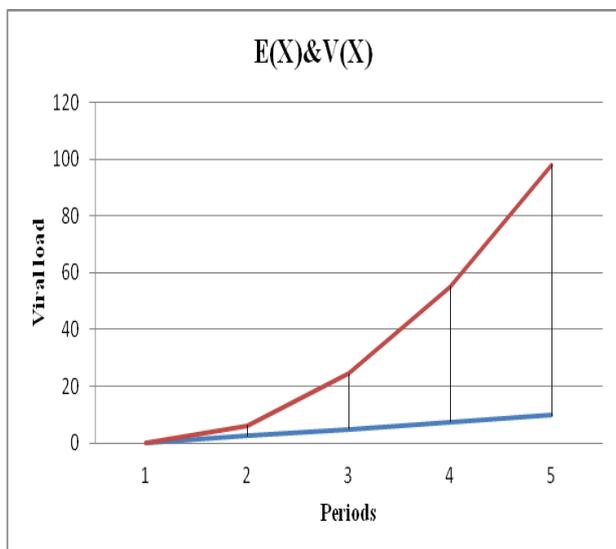


Graph I illustrate that viral load is increasing by assumption of branching process in pgf growth rate of replication. Whenever the periods increase, the viral load also increases.

Table:2 values of mean and variance for the Poisson distribution with $G(s) = 2.4741$ using $k = 5$

| periods | mean | variance |
|---------|--------|----------|
| 1 | 0 | 0 |
| 2 | 2.4741 | 6.1212 |
| 3 | 4.9482 | 24.4847 |
| 4 | 7.4223 | 55.0905 |
| 5 | 9.8964 | 97.9387 |

GRAPH: II



Graph II illustrate that viral load is increasing by assumption of branching process in pgf mean and variance growth rate of replication. Whenever the periods increase, the viral load also increases.

Exponential logarithmic application:

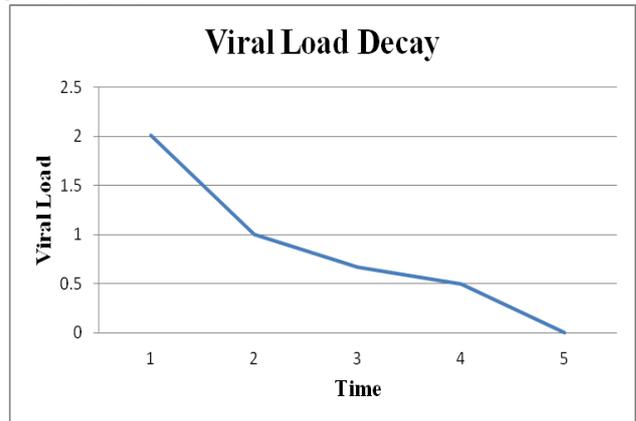
An ART therapy reduces a population of 10000 HIV viral loads to 97.9387 in 12 days.

Find the rate of decline caused by the ART $A = Pe^{rt}$

Table:3

| 12 days | Viral load decay |
|---------|------------------|
| 1 | 2.0066 |
| 2 | 1.0033 |
| 3 | 0.6688 |
| 4 | 0.5016 |
| 5 | 0.0017 |

GRAPH: III

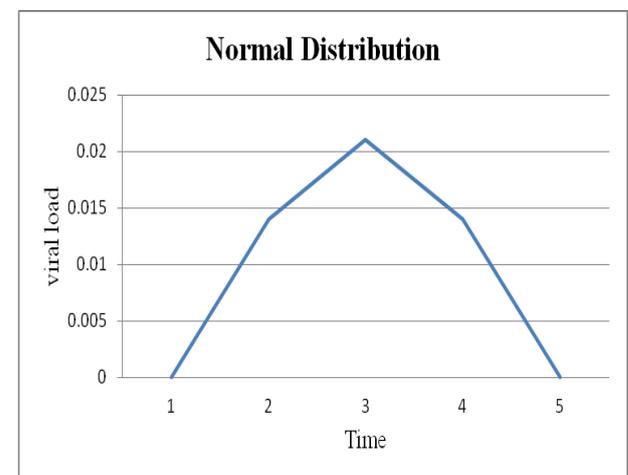


Graph III illustrate that viral load is decreasing by assumption of Exponential logarithmic application. Whenever the periods increase, the viral load decreases.

TABLE:4 The variation of viral load follows the normal distribution from this we identify the infection is increased.

| Time periods | Normal distribution |
|--------------|---------------------|
| 1 | 0 |
| 2 | 0.0140 |
| 3 | 0.0210 |
| 4 | 0.0140 |
| 5 | 0 |

GRAPH: IV



The above graph IV illustrate that the variation of viral load follows the normal distribution from this we identify the viral load decreasing.

IV. CONCLUSION

In this paper, the viral load function has been drawn using the branching process. An example has been also illustrated for viral load for different time periods with special case $\lambda = 2, P = 1, n = 5$ and also exponential logarithmic application has been draw to the example.

REFERENCES

1. Jun Liu , Yan Wang , Luju Liu , and Tingting Zhao 2018 ,A Stochastic HIV Infection Model with Latent Infection and Antiretroviral Therapy, Hindawi ,Discrete Dynamics in Nature and Society,Volume 2018, Article ID 5175383, 14 pages.
2. E.O. Romero-Seversona, G.D. Meadorsb, and E.M. Volzc, 2016,A generating function approach to HIV transmission with dynamic contact rates, HHS Public Access Author manuscript, Published in final edited form as: Math Model Nat Phenom. 2014 March 1; 9(2): 121–135. doi:10.1051/mmnp/20149208.
3. Andrei Y. Yakovlev, Vessela K. Stoimenova and Nikolay M. Yanev, Branching Processes as Models of Progenitor Cell Populations and Estimation of the Offspring Distributions,Journal of the American Statistical Association, Vol. 103, No. 484 (Dec., 2008), pp.1357-1366,Taylor & Francis, Ltd. on behalf of the American Statistical Association.
4. Andrei Yakovlev , Nikolai Yanev, 2006 Branching stochastic processes with immigration in analysis of renewing cell populations, Mathematical Biosciences 203 (2006) 37–63.
5. Ruy M. Ribeiro, Li Qin, Leslie L. Chavez, Dongfeng Li, Steven G. Self, And Alan S. Perelson,2010, Estimation Of The Initial Viral Growth Rate And Basic Reproductive Number During Acute Hiv-1 Infection, Journal Of Virology, June 2010, P. 6096–6102 Vol. 84, No. 120022-538x/10/\$12.00 Doi:10.1128/Jvi.00127-10.
6. Dominik Wodarz, and David N. Levy, 2011, Effect of different modes of viral spread on the dynamics of multiply infected cells in human immunodeficiency virus infection, This journal is q 2010 The Royal Society, J. R. Soc. Interface (2011) 8, 289–300 doi:10.1098/rsif.2010.0266.
7. Deborah Cromer, Mykola Pinkevych, Thomas A. Rasmussen, Sharon R. Lewin, Stephen J. Kent, Miles P. Davenporta, 2017, Modeling of Antilatenacy Treatment in HIV: What Is the Optimal Duration of Antiretroviral Therapy-Free HIV Remission?, American Society for Microbiology.,
8. David Wick, Steven G. Self, 2000, Early HIV infection in vivo: branching-process model for studying timing of immune responses and drug therapy, Mathematical Biosciences 165 (2000) 115±134, 0025-5564/00/\$ - see front matter Ó 2000 Elsevier Science Inc.
9. P. Layne, Micah Dembo, and John L. Spouge, The Kinetics of HIV Infectivity, Los Alamos Science Fall 1989.
10. B. Krishna Kumar, 2015, Branching Processes and Their Applications, Stochastic Modelling in Physical and Biological Sciences VTU & IASST, Guwahati, 5-7, February 2015. pp. Ch.5: 105-134.
11. J. E. Björnberg, T. Britton, E. I. Broman, And E. Natan, 2013, A Stochastic Model For Virus Growth In A Cell Population, Corresponding Author: E. I. Broman, Dept. Of Mathematics, Uppsala University, Box 256, 751 05 Uppsala, Sweden.
12. John William Bishir, 1961, Two Problems In The Theory Of Stochastic Branching Processes, Institute Of. Statistics Mimeograph Series No. 286 April, 1961.
13. Abid Ali Lashari, Pieter Trapman, 2018, Branching process approach for epidemics in dynamic partnership network, J. Math. Biol. (2018) 76:265–294.
14. D. Dolgopyat, P. Hebbar, L. Korolov, M. Perlman,(2018) Multi-Type Branching Processes With Time-Dependent Branching Rates applied Probability Trust (25 October 2018).
15. N.John Britto,(2014) A Study on stochastic Models for HIV infection and Aids, International Journal of Computing Algorithm, Volume: 03, May 2014, Pages: 994-997.
16. Azam A. Imomov, (2014), Limit Properties of Transition Functions of Continuous-Time Markov Branching Processes, Hindawi Publishing Corporation International Journal of Stochastic Analysis Volume 2014, Article ID 409345, 10 pages.
17. T. E. Harris, Some Mathematical Models For Branching Processes, The Rand Corporation, Second Berkeley Symposium: Harris.
18. G. Meenakshi and S. Saranya ,(2018), Stochastic Modeling of Viral Replication and Lysing CD4+T Cells in the HIV Infection International Journal of Scientific Research in Mathematical and Statistical Sciences Research in Research Paper, Volume-5, Issue-5, pp.243-252, October (2018) E-ISSN: 2348-4519.
19. Giuseppe Di Biase, Guglielmo D’Amico, Arturo Di Girolamo, Jacques Janssen,Stefano Iacobelli, Nicola Tinari, and Raimondo Manca, 2007, A Stochastic Model for the HIV/AIDS Dynamic Evolution, Hindawi Publishing Corporation,Mathematical Problems in Engineering, Volume 2007, Article ID 65636, 14 pages,doi:10.1155/2007/65636.
20. G.Meenakshi and P.R.Maheswari,(2019),prediction of HIV Replication in the Human Immune System using Multinomial Distribution by Bayesian methodology, International Journal of Scientific Research in Mathematical and Statistical Sciences, Research Paper, Volume-6, Issue-1, pp.46-52,February (2019) E-ISSN: 2348-4519.