

A Study on stochastic Models for HIV infection and Aids

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Abstract - This paper is review the Epidemiological modeling on threshold measuring measurement using probability and Mathematical Statistics.Mathematical models which would estimate the probable longevity of the infected and the extent of the usefulness of preventive measures Mathematical models that are purely threshold developed with less viability of applications.Some of the important and theoretical models developed include in the review.

Keywords: Threshold, Cumulative Shock Model, Non homogenous Poisson process, Bayesian Inference

I.INTRODUCTION

Nowak and May(1991) have discussed the effect of antigenic variation in the HIV infection and spread. The parasites(Virus) generate(Virus) generate the capacity to escape the antibiotics by the so called process of mutation. Therefore the newly produced .HIV possess-greater capacity to survive against the antibiotics, which are generated by the immune system to fight against the virus.

Any mathematical model is developed under some basic biological assumptions. The basic mathematical model is to find out the Quantitative consequeness to the antigenic diversity of HIV. The antigenic diversity threshold is by Stilianakis et.al(1994). In this paper, the authors have stated that as a retrovirus HIV shows a high replication error rate and leads to the creation of Distinct viral genomes with different immunological properties. This model predicts unrestrained HIV replication and depletion of T helper cells.This is believed to underlie the development of AIDS.

Boer et.al(1994) have brought out a mathematical model to determine the level of interaction between viral and antigenic diversity. The equilibrium between the above two is obtained using differential equation.

Krischner et al(2000) is one which deals with the causes and the rate at which the CD4+T cell eliminataion per unit of time takes place in HIV infected individuals. The author have introduced a new concept called the "homing process" and also apoptosis. According to the authors, in HIV infected patients.

Esay et al(1973), with the underlying process generating shocks as Poisson process, non homogeneous Poisson process respectively. Gerald(1955) , discussed the simple example of correlated interarrival time is assumed as exponentially distributed.

A slight modification of the Lack of Memory Property(LAM) has been suggested by Raja Rao and Talawaker(1990), the property is called Setting the clock

back to zero property(SCBZ), initially introduced by Stangle(1955) about Shock Model and cumulative process, which has been

Discussed by Suresh Kumar (2006),Kirchnes and Cloyd(2000) have developed a Mathematical model to describe the disease progression of HIV infected and the depletion ofCD4T-cell count which is turn have the interaction with the antigenic diversity. Sathiyamoorthi and Kannan (1998) have discussed a Stochastic model for estimating the expected time to seroconversion.

2.Methods and Materials

According to the author s in HIV infected patients, the decline of CD4+lymphocytes, can be described by three possible mechanisms.

(i)New CD4 lymphocytes are not generated at or above the normal rate

(ii) CD4+T cells are being killed in the blood and cleared.

(iii) The circulation patterns of CD4+T cells in the blood are alerted by increasing homing out of blood into tissues.

II.PRELIMINARY CONCEPTS

The following are some of the basic , existing and also recently developed concepts in Mathematical Statistics and Probability theory that are used to develop some stochastic models that are discussed as follows:

Cumulative damage model: Stochastic approach

The concept of shock models and cumulative damage process is an attractive one which helps in the interpretation of the behavior of complexmechanisms. Any component or device when expressed to shocks which cause damage to the device or system is likely to fail when the total accumulateddamage exceeds a level called the threshold. The rate of accumulation of damage determines the life time of the component or device. The inter-arrivaltimes between successive shocks also plays a role on the life time also the threshold levels as random variables, the expected time of failures of thedevice can be determined.

Assuming F(.) to be the distribution function of the random variable denoting the inter-arrival times between shocks, the threshold distribution as G(.), it can be shown that the probability the device survives k damage is denoted as

$$\bar{F}_k = \int_{-\infty}^{\infty} F(x).dG(x), \quad k = 1,2, \dots$$

Where, F(x) is the k-fold convolution of F(x) with itself and F(x) with itself and F0(x) =1, for x > 0 and 0, otherwise. The reliability R(t) of the devices in R(t) = $\sum_{k=0}^{\infty} \bar{F}_k \cdot v_k(t)$, where v(t) is the probability that k damages are caused during (o,t] , The above model has been considered by Esay et.al(1973), with the underlying

Process generating shocks as Poisson process, non homogeneous Poisson process and birth process respectively.

Distribution of sum of correlated random variables Generally in cumulative shock models the usual assumption is that the interarrival times of shocks are i.i.d random variables. But an exception is that to assume that the inter arrival times of shocks are identically idependently distributed random variables. But an exception is that the interarrival times of shocks are correlated, in the sense that the length of one such time interval between two successive shocks may be Correlated, to the next interarrival time. Such an assumption seems to be plausible in the case of inter contact times of sexually active partners especially when one of them is suspected to be infected by HIV. The uninfected partner, may under such a suspicion, tend to postpone further contracts. Gerald (1955) discussed inter arrival time are exponentially distributed and constantly correlated.

The characteristic function $\varphi(\lambda_1, \lambda_2, \dots, \lambda_n)$ of the joint distribution of any n random variables random variables from a sequence $\{x_n\}$ of exchangeable random variable each following the exponential distribution with p.d.f $f(x) = 1/ae^{-x/a}$ such that the correlation co-efficient R between $a > 0, 0 < x < X$ and X , and

$$Q(\lambda_1, \lambda_2, \dots, \lambda_n) = \begin{vmatrix} 1 - iaR & -iaR & \dots & -iaR \\ -iaR & 1 - iaR & \dots & -iaR \\ \dots & \dots & \dots & \dots \\ -iaR & -iaR & \dots & 1 - iaR \end{vmatrix}$$

Which is the Characteristics function

A Sequence $x_n, n=1,2,\dots$ random variables is called a sequence of exchangeable random variables, if the joint distribution $F_n(x_1, X_2, \dots, x_n)$ of any n random variables can be expressed

$$\text{as } F_n(x_1, X_2, \dots, x_n) = \int_{-\infty}^{\infty} G_w(x_1) \dots G_w(x_n), n = 1, 2, \dots, n.$$

Where $G_w(x_n)$ is conditional distribution function in X for each w and a random variable in

W for a given x. Here Ω is the space of W.

Setting the Clock Back to Zero property(SCBZ)

In Stochastic processes we can consider a sequence of random variable. Each random variables has an associated probability distribution. So, the probability density function of random variable X is denoted as $f(x)$. The corresponding distribution function is denoted as $F(x)$; and $S(X)=1-F(x)$ is called the survivor Function. For any probability distribution, there Correspondingly one or more parameters. For example, if a random variable x is distributed with Parameter Q, then we write it as x follows $f(x,Q) = Q.e^{-Qx}$. There is a property called the Lack of Memory property(LMP), Which says that the life time of a component like that of an electric bulb is such that the past length of life time completed by the component has no influence on the probability of instantaneous failure of the component in the function the exponential distribution satisfies this property. A slight modification satisfies this property has been suggested by Raja Rao and Talawaker(1990). This property is called the setting the clock back to Zero property(SCBZ) A family of life

distribution $f(x, \theta), x \geq 0, \theta \in \eta$, is said to have the "Setting the Clock Back to Zero"

Property is of the form of $f(x,Q)$ remains unchanged expect for the parameter under the three operations

- (i) Truncating the original distribution of some point $x_0 \geq 0$
- (ii) Considering the observable distributions for life time $x \geq x_0$ and
- (iii) Changing the origin by means of the transformation given by $x_1 = x - x_0, x_1 \geq x_0$

This property can be used to define some random variables, which are involved in the model.

According to this property, the probability distribution of the random variable X undergoesa change of parameter after a particular value of X denoted as x, known as truncation point.

So, the p.d.f of x is $f(x,Q)$ whenever X is less than or equal to x and it is $f(x, Q)$, whenever X is less than or equal to x and it is $f(x,Q)$ whenever $X > x$. This property is Indicted by a condition denoted as follows;

$$S(x+x_0, Q_1, Q_2)/S(x, Q_1) = S(x, Q_2), \text{ Where } s(x_1, Q) \text{ is the survival function}$$

Change of Distribution at a change point.

The SCBZ property is one in which case a random variable x has a parameter change after a certain value of x say x, which is called the truncation point. But there may be occasions where the random variable x has a probability density function $f(x)$ with cumulative distribution function $H(x)$. Here x is called the change point if x and after that it has probability density function $h(x)$ with cumulative distribution function

III. H(X) IS CHANGE POINT.THE CONCEPT OF CHANGE OF DISTRIBUTION IS AS FOLLOWS:

Let Y be a random variable in the probability density function $h(y)$ such that

$$H(y) = h_1(y) \text{ if } y \leq t$$

$$H_2(y) \text{ if } y > t \text{ and } h_2(y) = H_1(t)h_2(y - t)$$

and $\bar{H}(y) = 1 - H(t), H_1(t)$ being the cumulative distribution and is called change point.

Eg(1) If $h(y)$ follows exponential distribution with parameter Q and $h_2(y - t)$ follows

Erlang 2 distribution with parameter

$$\text{Then, } h(y) = \begin{cases} \theta_1 e^{-\theta_1 y}, & 0 < y \leq t \\ \theta_2^2 (y - t) e^{-\theta_2 (y - t)}, & y > t \end{cases}$$

The random variable X has the p.d.f $f(x)$ and c.d.f $F(x)$ whenever $X \leq x_0$ and it has the p.d.f $h(x)$ With c.d.f $H(X)$ whenever $x > x_0$. Here x_0 is called the change point.

$$\text{It can be noted that, } \int_0^{x_0} f(x) dx + \int_{x_0}^{\infty} h(x) dx = 1$$

Shock Model and cumulative Damage Process

A sequence of shocks occur randomly in time and the instantaneous damage occurring at the random epochs cumulative to an unknown threshold value beyond which the system fails itself a random variable. At every shock a random amount of damage is successive shocks get added together in the form of a cumulative damage. The rate at which the threshold is approached is to be studied. There are various approach to the rate of accumulation of

damage, but they all appear to be resolved in terms of the stochastic process. If the damages caused by successive shocks are i.i.d random variables denoted as X_i , $i=1,2,3, \dots,n$ with common Distribution function $G(\cdot)$, then the probability that the device survives k changes is denoted as: $P_k(x) = \int_0^{\infty} F_k(x)dx$, $k = 1, 2, \dots$ Where $F(x)$ is the k -fold convolution $f(x)$ with itself and $F_0(X)=1$. The reliability $R(t)$ of the device is given by, $R(t) = \int_0^{\infty} F_k(x)v_k(t)$, Where $V(t)$ is the probability that k damages are caused density $(o,t]$. The above model has been studied by Esayet al(1973) with the underlying generating the shock as poisson.

Reliability Function

Let T be a continuous random variable representing a lifetime characteristics, say time to fuse of device (component) is said to be reliable. If it is capable of performing its intended function adequately over a specified period of time. The statistical analysis of failure time data (Reliability study) as (i) Reliability function, $\bar{F}(x) = P(x > x)$, $x > 0$

$= 1 - F(x)$

(ii) Failure rate (hazard rate) $= \bar{F}(x) = \exp\left\{-\int_0^x h(t)dt\right\}$

(iii) Mean residual life function $\bar{F}(x) = \frac{r(0)}{r(x)} \cdot e^{\int_0^x \frac{1}{r(t)} dt}$

Exponential distribution

The one-parameter exponential distribution has the following density function

$f(t) = \lambda e^{-\lambda t}$

$F(t) = 1 - e^{-\lambda t}$

Survivorship function $S(t) = e^{-\lambda t}$

Hazard function $h(t) = \lambda$

Where $t \geq 0, \lambda > 0$, obviously, the exponential distribution is one parameter λ

Geometric Process

Let $E(t), t > 0$ be a counting process and let $u_n, n=1,2, \dots$ be a sequence of non-negative independent random variables. The distribution function of u is denoted as B . $B(a_{n-1}, t)$, $n=1,2, \dots,k$, where a is a positive constant. If then the waiting process is called a geometric process. Here T is called the n^{th} change inter arrival time

IV. CONCLUSION

Philip (1996) considers random variable n number of CD4+T cell count over a period is distributed as poisson. Then find whether generated is damaged cell is x is distributed as compound poisson process.

$$P(x=r / n = k) = P(x=r / n = k) p(n = k)$$

$$= \frac{e^{-\lambda} \lambda^k}{k!} \binom{k}{j} p^r q^{k-r}$$

Therefore, the marginal distribution of x , the number of damaged cells over the period is given by

$$P(x=r) = \sum_{k=r}^{\infty} p(x = r \cap x = k) = \frac{e^{-\lambda p} (\lambda p)^r}{r!}$$
 so the average of

the number of damaged CD4+T cells a time interval at λp .

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