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A stochastic approach to determine expected time to seroconversion when the intercontact times form a geometric process

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Abstract

The study of HIV infection, transmission and spread of AIDS is quite common by the use of stochastic model. The estimation of expected time to seroconversion of HIV infected over the time interval (0, t] is an important aspects which help medical intervention. In this paper focuses on the study of a stochastic model for predicting the seroconversion time when the intercontact times form a geometric process using geometric distribution as the threshold. In this study the theoretical results are substantiated by using numerical data simulated.

Keywords: Acquired Immuno Deficiency Syndrome, Human Immuno-deficiency Virus, Seroconversion, Antigenic Diversity Threshold and Geometric Process

Introduction

In the study of HIV infection and its progression, the antigenic diversity of the antigen namely the HIV plays an important role. The intensity of sexual contact is an important factor that adds to the antigenic diversity since more number of new antigens are acquired by the individual who is getting infected. The time to seroconversion from the point of infection depends upon what is known as antigenic diversity, which acts against immune ability of an individual. Every individual has a threshold level of antigenic diversity. If the antigenic diversity due to acquiring more and more HIV due to homo or heterosexual contacts exceeds the threshold level, the immune system of human body is completely suppressed which in turn leads to seroconversion. Mathematical methods have been developed by Nowak and May (1991), Stilianakis *et al.* (1994) and Kirschner *et al.* (2000) developed suitable model to estimate the antigenic diversity threshold. Sathiyamoorthi and Kannan (2001) used the shock model and cumulative damage process evolved by Esary *et al.* (1973) to estimate the expected time to cross the antigenic diversity threshold.

In the estimation of expected time to seroconversion there is an important role for interarrival times between successive contacts; and it has a significant influence. In the case of persons exposed to HIV infection through sexual contacts, the contribution to the antigenic diversity would depend upon the number of contacts in the interval (0, t]. If any person has contact with an unknown partner is likely to have the fear of getting infected. However the person does not avoid the contacts. But there is a possibility that a person may postpone the event namely the contact due to the fear complex. This gives rise to the sequence of random variables in increasing order. Therefore it is considered here that the interarrival times between contacts may form a geometric process.

In this paper a stochastic model to determine the expected time to seroconversion and its variance are discussed under the assumption that interarrival times between contacts are distributed as a geometric process using geometric distribution as a threshold. For detailed study of geometric process and its property one can refer to Lam Yeh (1988). In this study the theoretical results are substantiated using numerical data simulated.

Assumptions of the Model

- The transmission of HIV only through sexual contacts.
- An uninfected individual has sexual contacts with a HIV infected partner and in every contact a random number of HIV are transmitted.
- The interarrival times between successive contacts are random variables which form a geometric process.
- The sequence of successive contacts and threshold level are independent.
- The total damage exceeds a threshold level Y, which itself is a random variable, the seroconversion occurs and a person is recognized as seropositive.

Notations

X_i : a random variable denoting the increase in the antigenic diversity arising due to the HIV transmitted during the i^{th} contact and X_i's are i.i.d. for i = 1,2,…,k.

Y : a random variable representing antigenic diversity threshold follows geometric distribution with parameter θ.

T : a random variable denoting the time to seroconversion .

U_i : a random variable denoting the interarrival times between successive contacts with p.d.f. b(.).

G(X) : The c.d.f of X by taking $X_i = X$ for i = 1,2,…,k and g(x) the corresponding p.d.f.

P'_n : $P\lfloor X_i = n \rfloor$, the probability that 'n' particles of HIV are transmitted during the i^{th} contact.

$\psi(s)$: $\sum_{n=1}^{\infty} p'_n s^n$, the p.g.f of X.

$V_k(t)$: probability of exactly k contacts in (0, t].

$\bar{\theta}$: 1 - θ.

Results

It can be shown that

$$S(t) = P\,[T > t]$$

$$= \sum_{k=0}^{\infty} V_k(t) P\left[\sum_{i=1}^{k} X_i < Y\right] \quad \dots (1)$$

$$= \sum_{k=0}^{\infty} P\{\text{exactly k contacts in } (0,t]\} \times P\{\text{no seroconversion in k contacts}\}$$

Now

$$P[Y > n] = \sum_{i=1}^{\infty} P[Y = n+i]$$

$$= \sum_{i=1}^{\infty} \bar{\theta}^{\,n+i-1}\,\theta$$

$$P[Y > n] = \bar{\theta}^{\,n}$$

This gives

$$P\left[\sum_{i=1}^{k} X_i < Y\right] = \sum_{n} P\left(\sum_{i=1}^{k} X_i = n\right) P(Y > n)$$

$$= \sum_{n} P\left(\sum_{i=1}^{k} X_i = n\right) \bar{\theta}^{\,n}$$

$$= \sum_{n=1}^{\infty} p_n^{t}\, \bar{\theta}^{\,n} = [\psi(\bar{\theta})]^k$$

From equation (7.1), we get

$$S(t) = \sum_{k=0}^{\infty} [B_k(t) - B_{k+1}(t)]\; [\psi(\bar{\theta})]^k$$

$$L(t) = 1 - S(t)$$

$$= 1 - \sum_{k=0}^{\infty} [B_k(t) - B_{k+1}(t)]\; [\psi(\bar{\theta})]^k$$

$$L(t) = [1 - \psi(\bar{\theta})] \sum_{k=1}^{\infty} B_k(t)\; [\psi(\bar{\theta})]^{k-1}$$

On simplification

Hence

$$L(t) = [1 - \psi(\bar{\theta})] \sum_{n=1}^{\infty} B_n(t)\; [\psi(\bar{\theta})]^{n-1}$$

The p.d.f. as

$$l(t) = [1 - \psi(\bar{\theta})] \sum_{n=1}^{\infty} b_n(t)\; [\psi(\bar{\theta})]^{n-1}$$

The Laplace transform of $l(t)$

$$l^*(s) = [1 - \psi(\bar{\theta})] \sum_{n=1}^{\infty} b_n^*(s)\; [\psi(\bar{\theta})]^{n-1}$$

Since $U_i^{'}s$ form a geometric process $b_n^*(s)$ can be written as

$$b_n^*(s) = \prod_{k=1}^{n} b^*\left(\frac{s}{a^{k-1}}\right)$$

Hence

$$l^*(s) = [1 - \psi(\bar{\theta})] \sum_{n=1}^{\infty} [\psi(\bar{\theta})]^{n-1} \prod_{k=1}^{n} b^*\left(\frac{s}{a^{k-1}}\right)$$

Consider

$$b_n^*(s) = \prod_{k=1}^{n} b^*\left(\frac{s}{a^{k-1}}\right)$$

$$= b^*(s).b^*\left(\frac{s}{a}\right).b^*\left(\frac{s}{a^2}\right).b^*\left(\frac{s}{a^3}\right)\cdots b^*\left(\frac{s}{a^{n-1}}\right)$$

$$\frac{d}{ds}\left[b_n^*(s)\right]\Big|_{s=0} = \frac{d}{ds}\left[b^*(s).b^*\left(\frac{s}{a}\right).b^*\left(\frac{s}{a^2}\right).b^*\left(\frac{s}{a^3}\right)\cdots b^*\left(\frac{s}{a^{n-1}}\right)\right]\Big|_{s=0}$$

$$= \left\{b^{*\prime}(s).b^*\left(\frac{s}{a}\right).b^*\left(\frac{s}{a^2}\right)\cdots b^*\left(\frac{s}{a^{n-1}}\right) + b^*(s).b^{*\prime}\left(\frac{s}{a}\right)\frac{1}{a}.b^*\left(\frac{s}{a^2}\right)\cdots b^*\left(\frac{s}{a^{n-1}}\right)\right.$$

$$\left. + \; b^*(s).b^*\left(\frac{s}{a}\right).b^{*\prime}\left(\frac{s}{a^2}\right)\frac{1}{a^2}\cdots b^*\left(\frac{s}{a^{n-1}}\right) + \cdots + b^*(s).b^*\left(\frac{s}{a}\right).b^*\left(\frac{s}{a^2}\right)\cdots b^{*\prime}\left(\frac{s}{a^{n-1}}\right)\frac{1}{a^{n-1}}\right\}$$

and at s = 0

$$= b^{*\prime}(0) + b^{*\prime}(0).\frac{1}{a} + b^{*\prime}(0).\frac{1}{a^2} + \cdots + b^{*\prime}(0).\frac{1}{a^{n-1}}$$

$$= b^{*\prime}(0)\left\{1 + \frac{1}{a} + \frac{1}{a^2} + \cdots + \frac{1}{a^{n-1}}\right\}$$

Hence

$$b_n^{*\prime}(0) = b^{*\prime}(0)\left[\frac{a^n - 1}{(a-1)a^{n-1}}\right]$$ On simplification

$$E(T) = -\frac{dl^*(s)}{ds}\Big|_{s=0}$$

$$= -\left[1-\psi(\bar{\theta})\right]\sum_{n=1}^{\infty} b_n^{*\prime}(0)\left[\psi(\bar{\theta})\right]^{n-1}$$

$$= -\left[1-\psi(\bar{\theta})\right]\sum_{n=1}^{\infty}\left[\psi(\bar{\theta})\right]^{n-1} b^{*\prime}(0)\left[\frac{a^n - 1}{(a-1)a^{n-1}}\right]$$

$$E(T) = -\frac{b^{*\prime}(0)\,a}{[a - \psi(\bar{\theta})]}$$ On simplification … (2)

Assuming b(.) ~ exp(μ), then

$$b^*(s) = \frac{\mu}{\mu + s}$$

Therefore

$$b^{*\prime}(0) = \frac{db^*(s)}{ds}\Big|_{s=0} = -\frac{1}{\mu} \quad \ldots (3)$$

$$b^{*\prime\prime}(0) = \frac{d^2b^*(s)}{ds^2}\Big|_{s=0} = \frac{2}{\mu^2} \quad \ldots (4)$$

Substituting equation (3) in (2)

$$E(T) = \frac{a}{\mu[\, a - \psi(\bar{\theta})]}$$

$$\left.\frac{d^2 b_n^*(s)}{ds^2}\right|_{s=0} = \frac{d}{ds}\left\{ b^{*\prime}(s).\, b^*\left(\frac{s}{a}\right).\, b^*\left(\frac{s}{a^2}\right).\ \cdots b^*\left(\frac{s}{a^{n-1}}\right)\right.$$

$$+ b^*(s).\, b^{*\prime}\left(\frac{s}{a}\right)\frac{1}{a}.\ b^*\left(\frac{s}{a^2}\right).\ \cdots b^*\left(\frac{s}{a^{n-1}}\right)$$

$$+ b^*(s).\, b^*\left(\frac{s}{a}\right).\ b^{*\prime}\left(\frac{s}{a^2}\right)\frac{1}{a^2}.\ \cdots b^*\left(\frac{s}{a^{n-1}}\right)$$

$$\left. + \cdots + b^*(s).\, b^*\left(\frac{s}{a}\right).\ b^*\left(\frac{s}{a^2}\right).\ \cdots b^{*\prime}\left(\frac{s}{a^{n-1}}\right)\frac{1}{a^{n-1}}\right\}$$

$$= \left\{ b^{*\prime\prime}(0) - \left[b^{*\prime}(0)\right]^2 \right\}\left\{\frac{1 - \frac{1}{a^{2n}}}{1 - \frac{1}{a^2}}\right\} + \left[b^{*\prime}(0)\right]^2 \left\{\frac{a^n - 1}{(a-1)a^{n-1}}\right\} \quad \left\{\frac{a^n - 1}{(a-1)a^{n-1}}\right\}$$

$$= \left\{ b^{*\prime\prime}(0) - \left[b^{*\prime}(0)\right]^2 \right\}\left\{\frac{a^{2n} - 1}{a^{2n}a^{-2}(a^2 - 1)}\right\} + \left[b^{*\prime}(0)\right]^2 \left\{\frac{a^n a^n - a^n - a^n + 1}{(a-1)^2 a^{n-1}\, a^{n-1}}\right\}$$

Hence

$$b_n^{*\prime\prime}(0) = \left\{ b^{*\prime\prime}(0) - \left[b^{*\prime}(0)\right]^2 \right\}\left\{\frac{a^{2n} - 1}{a^{2(n-1)}(a^2 - 1)}\right\} + \left[b^{*\prime}(0)\right]^2 \left\{\frac{a^{2n} - 2a^n + 1}{(a-1)^2 a^{2(n-1)}}\right\}$$

On simplification … (5)

$$E(T^2) = \left.\frac{d^2 l^*(s)}{ds^2}\right|_{s=0}$$

$$= \left[1 - \psi(\bar{\theta})\right] \sum_{n=1}^{\infty} \left[\psi(\bar{\theta})\right]^{n-1} b_n^{*\prime\prime}(0) \qquad \ldots (6)$$

Substituting equation (5) in (6)

$$= \left[1 - \psi(\bar{\theta})\right]\left\{ b^{*\prime\prime}(0) - \left[b^{*\prime}(0)\right]^2 \right\}\sum_{n=1}^{\infty}\left[\psi(\bar{\theta})\right]^{n-1}\left\{\frac{a^{2n} - 1}{a^{2(n-1)}(a^2 - 1)}\right\}$$

$$+ \left[1 - \psi(\bar{\theta})\right]\left[b^{*\prime}(0)\right]^2 \sum_{n=1}^{\infty}\left[\psi(\bar{\theta})\right]^{n-1}\left\{\frac{a^{2n} - 2a^n + 1}{(a-1)^2 a^{2(n-1)}}\right\}$$

$$E(T^2) = \frac{a^2\left\{ b^{*\prime\prime}(0) - \left[b^{*\prime}(0)\right]^2 \right\}}{\left[a^2 - \psi(\bar{\theta})\right]} + \frac{a^2\left[b^{*\prime}(0)\right]^2 \left[a + \psi(\bar{\theta})\right]}{\left[a - \psi(\bar{\theta})\right]\left[a^2 - \psi(\bar{\theta})\right]}$$ On simplification

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

$$= \frac{a^2\left\{ b^{*\prime\prime}(0) - \left[b^{*\prime}(0)\right]^2 \right\}}{[a^2 - \psi(\bar{\theta})]} + \frac{a^2\left[b^{*\prime}(0)\right]^2 \left[a + \psi(\bar{\theta})\right]}{[a - \psi(\bar{\theta})]\ [a^2 - \psi(\bar{\theta})]} - \left\{ - \frac{\left[b^{*\prime}(0)\, a\right]}{[a - \psi(\bar{\theta})]}\right\}^2$$

$$V(T) = \frac{a^2\left\{ b^{*\prime\prime}(0) - \left[b^{*\prime}(0)\right]^2 \right\}}{[a^2 - \psi(\bar{\theta})]} + \left[\frac{\left[b^{*\prime}(0)\right]^2 a^2\ \psi(\bar{\theta})\left[1 - \psi(\bar{\theta})\right]}{[a - \psi(\bar{\theta})]^2\ [a^2 - \psi(\bar{\theta})]}\right]$$ On simplification

Substituting (7.3) and (7.4) in V(T), we get

$$V(T)=\frac{a^2}{\mu^2[a^2-\psi(\bar{\theta})]}\left[1+\frac{\psi(\bar{\theta})\,[1-\psi(\bar{\theta})]}{[a-\psi(\bar{\theta})]^2}\right]$$

On simplification

Special case

If $P_n=\frac{e^{-\lambda}\lambda^n}{n!}$, then $\psi(\bar{\theta})=\sum_{n=1}^{\infty}\frac{e^{-\lambda}\lambda^n}{n!}\bar{\theta}^n=e^{-\lambda(2\bar{\theta}+1)}$

then

$$E(T)=\frac{a}{\mu\left[a-e^{-\lambda(3-2\theta)}\right]}$$

and

$$V(T)=\frac{a^2}{\mu^2\,[a^2-e^{-\lambda(3-2\theta)}]}\left\{1+\frac{e^{-\lambda(3-2\theta)}\left[1-e^{-\lambda(3-2\theta)}\right]}{\left[a-e^{-\lambda(3-2\theta)}\right]^2}\right\}$$

Numerical Illustrations

Table 1

a	$\mu = 1,\ \theta = 0.1, \lambda = 1$	
	E(T)	V(T)
1	1.0647	1.1336
2	1.0314	1.0308
3	1.0207	1.0134
4	1.0154	1.0075
5	1.0123	1.0047
6	1.0102	1.0033
7	1.0088	1.0024
8	1.0077	1.0018
9	1.0068	1.0015
10	1.0061	1.0012

Table 2

μ	$a = 2,\ \theta = 0.1, \lambda = 1$	
	E(T)	V(T)
1	1.0314	1.0308
2	0.5157	0.2577
3	0.3438	0.1146
4	0.2578	0.0645
5	0.2063	0.0412
6	0.1719	0.0286
7	0.1473	0.0210
8	0.1289	0.0161
9	0.1146	0.0127
10	0.1031	0.0104

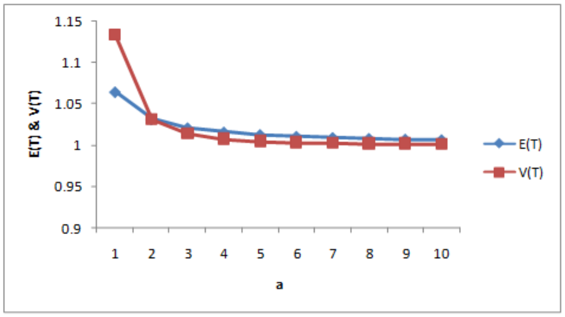

Figure 1

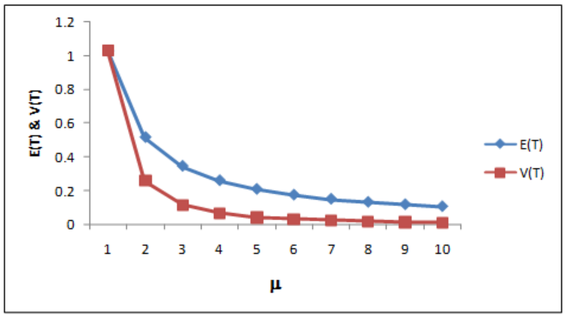

Figure 2

Table 3

θ	μ = 1, a = 2, λ = 1	
	E(T)	V(T)
0.1	1.0314	1.0308
0.2	1.0386	1.0377
0.3	1.0475	1.0463
0.4	1.0587	1.0569
0.5	1.0726	1.0699
0.6	1.0901	1.0858
0.7	1.1123	1.1056
0.8	1.1406	1.1301
0.9	1.1773	1.1602
1.0	1.2254	1.1973

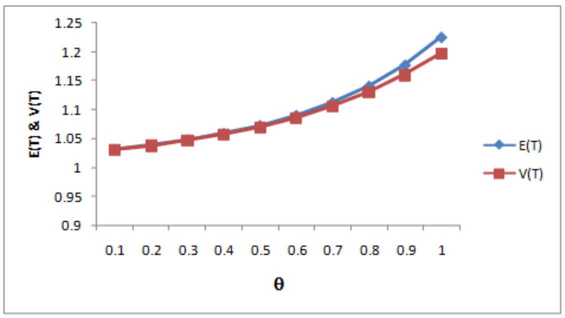

Figure 3

Table 4

λ	μ = 1, a = 2, θ = 0.1	
	E(T)	V(T)
1	2.0619	1.3025
2	1.2338	1.2036
3	1.0749	1.0721
4	1.0263	1.0259
5	1.0095	1.0094
6	1.0035	1.0034
7	1.0013	1.0012
8	1.0005	1.0004
9	1.0002	1.0000
10	1.0000	1.0000

Conclusions

It can be seen from Table 1 that as ‘a’ increases E(T) decreases. This is due to the fact that in a geometric process if a > 1 the sequence of random variables would be decreasing and so the interarrival time forms a decreasing sequence. Hence E(T) decreases, by the fact that the contact would be more frequent. Similarly the variance of the seroconversion time also decreases.

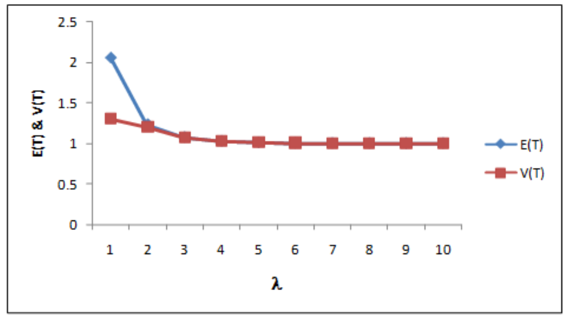

Figure 4

If μ the parameter of the distribution of the random variable, U_i denoting the intercontact time is increasing then expected time to seroconversion decreases. It is due to fact that since U_i follows exp(μ), $E(U_i) = \frac{1}{\mu}$.

Hence if μ increases then the interarrival times on the average decreases. Then there would be more number of contacts. Hence the expected time to seroconversion decreases and its variance also decreases as indicated in Table 2.

From the Table 3, it can be seen that as the parameter ‘θ’ of the threshold distribution increases, the mean time to seroconversion as well as the variance time to seroconversion increase.

As the value of the parameter λ of the random variables X_i, denoting the contribution to antigenic diversity increases both expected time to seroconversion and its variance also decrease as indicated in Table 4.

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