ESTIMATION OF EXPECTED TIME TO SEROCONVERSION OF HIV INFECTED WHEN INTERCONTACT TIMES ARE CORRELATED

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ABSTRACT

In the study of HIV infection and its progression to AIDS, the antigenic diversity of the invading antigens is an important aspect, the virulence of the invading antigen also undergoes changes due to successive contacts. The expected time to cross the antigenic diversity threshold of the human immune system has been estimated by using suitable stochastic models. Several variations of these models have been discussed. In this paper it is assumed that, the seroconversion takes place when the total antigenic diversity of the invading antigens (or) the total virulence crosses the respective threshold. An assumption is that the two events do not take place simultaneously. Numerical illustration is also discussed.

Keywords: HIV, AIDS, Seroconversion, Antigenic Diversity Threshold, Virulence Threshold

Introduction

The spread of HIV infection and consequent AIDS due to seroconversion is a matter of concern not only for those who are infected and also for the medical personnel who make efforts to provide medical care for those who are infected. It is also a cause of worry for the people in the governance of the country because it involves much of efforts and also expenditure.

To study the progression of HIV infection and also the time taken for the seroconversion of the infected people several mathematical stochastic models have been developed by several authors. These models, if applied to real life situations provide information regarding the time taken for seroconversion and also the time taken for manifestation of full blown AIDS symptoms. The concept of antigenic diversity threshold for AIDS patients is discussed in detail by Stilianakis et. al (1994). Nowak and May (1991) have discussed about the antigenic diversity threshold. Boer R.J et al (1994) have discussed about the concept of antigenic diversity and virulence threshold in AIDS. A stochastic model to
estimate the expected time to seroconversion has been discussed by Sathiyamoorthi and Kannan (2001). They have also discussed a stochastic model in which it is assumed that the inter contact times between the infected and non infected are random variables which are constantly correlated.

It is an interesting observation that in the process of seroconversion not only the antigenic diversity plays a vital role but also the virulence developed by the invading antigens. Virulence may be defined as the disease producing ability of a micro organism. There is evidence for heritable variation in viral traits that influence the virulence of the virus. The concept of antigenic diversity and virulence thresholds has been discussed by Nowak, et. al. (1994), Sabestian Bonho effer and Nowak (1994) have discussed the concept of mutation and evolution of virulence. The concept of obtaining the density function of sum of random variables which are exponentially distributed, constantly correlated and exchangeable has been discussed by Gurland (1995). In this paper the expected time to seroconversion assuming two thresholds namely antigenic diversity threshold and virulence threshold and also assuming that the inter arrival times between successive sexual contacts are random variables which are constantly correlated, exponential and exchangeable.

ASSUMPTIONS

1. A person is exposed to sexual contacts with an infected partner and on each occasion of contact the transmission of HIV takes place.
2. The mode of transmission of HIV on successive occasions results in the contribution to the antigenic diversity of the invading antigens. Also there is an increase in the virulence of the invading antigens.
3. As and when the total antigenic diversity crosses a particular level called the antigenic diversity threshold, then the seroconversion takes place. Similarly if the total virulence of the invading antigens crosses the virulence threshold, then the seroconversion will occur.
4. The crossing of both antigenic diversity threshold and virulence threshold simultaneously is considered to be an impossible event.
5. The two thresholds are random variables and are mutually independent.
6. The time interval between successive contacts are random variables which are inter correlated.

NOTATIONS

\[ X_i = \text{a random variable denoting the contribution to antigenic diversity on the } i^{\text{th}} \text{ contact } i = 1, 2, 3, \ldots, k \text{ and with p.d.f. } g(.) \text{ with c.d.f. } G(.) \]

\[ Y_i = \text{a random variable denoting the increase in the virulence due to the } i^{\text{th}} \text{ contact, } i = 1, 2, 3, \ldots, k \text{ with p.d.f. } q(.) \text{ and c.d.f. } Q(.) \]

\[ Z_1 = \text{a random variable denoting antigenic diversity threshold and has p.d.f. } h(.) \text{ and c.d.f. } H(.) \]

\[ Z_2 = \text{a random variable denoting the virulence threshold with p.d.f. } m(.) \text{ and c.d.f. } M(.) \]

\[ U_i = \text{a random variables denoting the time interarrival between successive contacts and } i = 1, 2, 3, \ldots, k. U_i's \text{ are exchangeable exponential random variables which are constantly correlated with p.d.f. } f(.) \text{ and c.d.f. } F(.) \]

\[ F_k(.) = \text{c.d.f of the partial sum of } X_1 + X_2 + X_3 + \ldots + X_k \]

\[ R = \text{Correlation between any } U_i, U_j, i \neq j \]

\[ T = \text{Time to seroconversion} \]
\[ L(t) = 1 - S(t) \text{ where } S(t) = P(T > t) \]
\[ b = a (1 - R) \]
\[ l^*(s) = \text{Laplace transform of } l(t). \]

**RESULTS**

\[ S(t) = P \left[ T > t \right] = P \left[ \text{The Total antigenic diversity due to 'k' contacts does not cross the threshold level and total virulence developed due to 'k' contacts does not cross the virulence threshold} \right]. \]

Hence \[ S(t) = P[\sum_{i=1}^{k} x_i < Z_1 \cap \sum_{i=1}^{k} y_i < Z_2] \]
\[ = P[\sum_{i=1}^{k} x_i < Z_1] \cdot P[\sum_{i=1}^{k} y_i < Z_2] \]
\[ = \text{Pr} \left[ \text{That there are k contacts in (0,t) and the total antigenic diversity does not cross the threshold and the total virulence does not cross the threshold} \right] \]

\[ S(t) = \sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)] \left[ \int_0^\infty g_k(x) \overline{H(x)} dx \right] \left[ \int_0^\infty q_k(y) \overline{M(y)} dy \right] \]
\[ = \sum_{k=0}^{\infty} [F_k(t) - F_{k+1}(t)] \left[ g^*_k(\theta) q^*_k(\lambda) \right] \]
\[ = 1 - \left[ 1 - g^*(\theta) q^*(\lambda) \right] \sum_{k=1}^{\infty} F_k(t) \left[ g^*(\theta) q^*(\lambda) \right]^{k-1} \]
\[ L(t) = 1 - S(t) \]
\[ = \left[ 1 - g^*(\theta) q^*(\lambda) \right] \sum_{k=1}^{\infty} F_k(t) \left[ g^*(\theta) q^*(\lambda) \right]^{k-1} \]

Taking Laplace transform of both sides we have
\[ l^*(s) = \left[ 1 - g^*(\theta) q^*(\lambda) \right] \sum_{k=1}^{\infty} F_k(s) \left[ g^*(\theta) q^*(\lambda) \right]^{k-1} \]

we assume that \[ f(.) \sim \text{exp}(\eta) \] and \[ f^*(s) = \frac{\eta}{\eta+s} \]
\[ g(.) \sim \exp(\beta) \quad \text{and} \quad g^*(\theta) = \frac{\beta}{\theta + \beta} \]

\[ q(.) \sim \exp(c) \quad \text{and} \quad q^*(\lambda) = \frac{c}{\lambda + c} \]

By using expression for \( F_k^*(s) \) and then \( f^*(s) \) due to Gurland (1955) we obtain the \( E(T) \) which means the expected time to seroconversion.

Now,

\[ f^*(s) = \left[ \frac{1}{(1+bs)^k} \right] \left[ \frac{1}{(1-R)(1+bs)} \right] \]

as described by Gurland (1955)

substituting this in equation (4) we get

\[ l^*(s) = \left[ 1 - g^*(\theta)q^*(\lambda) \right] \sum_{k=1}^{\infty} \frac{1}{(1+bs)^k} \left[ \frac{1}{kRbs} \right] \left[ g^*(\theta) q^*(\lambda) \right]^{k-1} \]  \[= \left[ 1 - g^*(\theta)q^*(\lambda) \right] \left[ g^*(\theta) q^*(\lambda) \right]^{k-1} \sum_{k=1}^{\infty} \frac{1}{(1+bs)^k} \left[ \frac{1}{kRbs} \right] \]  \[= \sum_{k=1}^{\infty} (1+bs)^{-k} (1-R)(1+bs)(1-R)(1+bs) + kRbs]^{-1} \]

\[ \sum_{k=1}^{\infty} (1+bs)^{-k} (1-R)(1+bs)(1-R)(1+bs) + kRbs]^{-1} \]

Diff. (7) w.r.t 's'

\[ \frac{dl^*(s)}{ds} = \frac{(1-R)(1+bs)^1-k (-1)[(1-R)(1+bs) + kRbs]^{-1-1}}{(1-R)(1-R)+b+kRb+1-R+b+RkRb=1-k^1+bs=0} \]

\[= \frac{(1-R)(1+bs)^1-k (-1)[(1-R)b + kRb] + [(1-R)(1)]^{-1}(1-k)(1)^{-k}.b}{(1-R)[(1-R)b + kRb] + [1-R]^{-1+1}(b-bk)} \]

\[= \frac{(1-R)[(1-R)b + kRb] + [1-R]^{-2}(1-R)(b-bk)}{(1-R)[(1-R)b + kRb] + [1-R]^{-2}(1-R)(b-bk)} \]

\[= \frac{-bk}{(1-R)} \]  \[= \frac{bk}{(1-R)} \]

On simplification

Substitute equ. (9) in equ. (6)

\[ 1 - g^*(\theta)q^*(\lambda) = 1 - \frac{\beta}{\beta + \theta} \cdot \frac{c}{c + \lambda} \]
\begin{align*}
1 - g^*(\theta)q^*(\lambda) &= \frac{\beta \lambda + \theta c + \theta \lambda}{\beta c + \beta \lambda + \theta c + \theta \lambda} \\
[g^*(\theta)q^*(\lambda)]^{k-1} &= \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^{k-1} \\
\end{align*}

Substituting equ. (9), equ. (10), equ. (11) in equ. (6) we get

\begin{align*}
\frac{\beta \lambda + \theta c + \theta \lambda}{\beta c + \beta \lambda + \theta c + \theta \lambda} \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^{k-1} \sum_{k=1}^{\infty} bk \\
= \frac{b(\beta \lambda + \theta c + \theta \lambda)}{(1-R)(\beta c + \beta \lambda + \theta c + \theta \lambda)} \sum_{k=1}^{\infty} k \left( \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right)^{k-1} \\
= \frac{b(\beta \lambda + \theta c + \theta \lambda)}{(1-R)(\beta c + \beta \lambda + \theta c + \theta \lambda)} \left[ 1 + 2 \left( \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right) + 3 \left( \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right)^2 + \ldots \ldots \right] \\
= \frac{b(\beta \lambda + \theta c + \theta \lambda)}{(1-R)(\beta c + \beta \lambda + \theta c + \theta \lambda)} \left[ 1 - \left( \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right)^{-2} \right] \\
= \frac{b(\beta \lambda + \theta c + \theta \lambda)}{(1-R)(\beta c + \beta \lambda + \theta c + \theta \lambda)} \left[ 1 - \frac{\beta c}{\beta c + \beta \lambda + \theta c + \theta \lambda} \right]^{-2} \\
= \frac{b(\beta \lambda + \theta c + \theta \lambda)}{(1-R)(\beta c + \beta \lambda + \theta c + \theta \lambda)} \left( \frac{\beta \lambda + \theta c + \theta \lambda}{\beta c + \beta \lambda + \theta c + \theta \lambda} \right)^{-2} \\
\end{align*}

On simplification

\begin{align*}
E(T) &= \frac{b(\beta c + \beta \lambda + \theta c + \theta \lambda)}{(1-R)(\beta c + \beta \lambda + \theta c + \theta \lambda)} \left\{ 1 - \left[ 1 - \left( \frac{\beta c}{\beta c + \beta \lambda + \theta c + \theta \lambda} \right)^{-2} \right] \right\} \\
\end{align*}

From equ. (8)

\begin{align*}
\frac{dI^*(s)}{ds} &= (1-R)\left\{ -(1+bs)^{1-k} \left[ (1-R)(1+bs) + kRbs \right]^{-2} \left[ (1-R)(b) + kRb \right] + [(1-R)(1+bs) + kRbs]^{-1+1} \right\} \\
&= (1-R)\left\{ -(1+bs)^{1-k} \left[ (1-R)(1+bs) + kRbs \right]^{-2} \left[ (1-R)(b) + kRb \right] + (1-R^{1+bs} + kRbs^-21-R^{1+bs} + kRb^{s^-2k}(1+bs)^{-k}) \right\} \\
&= (1-R)\left\{ (1+bs)^{-k} \left[ (1-R)(1+bs) + kRbs \right]^{-2} \left[ -(1+bs)(b-RbRb) \right] + ((1-R)(1+bs) + kRbs)(b-bk) \right\} \\
\end{align*}
\[ (1 - R) \{(1 + bs)^{-k} [(1 - R)(1 + bs) + kRbs]^{-2} \} \]

\[ + (1 + bs)^{-k} [(1 - R)(1 + bs) + kRbs]^{-2} \{- bk - b^2 sk + Rb^2 ks - k^2 b^2 Rs \}] \]

\[ = (1 - R)\{(1 + bs)^{-k} [(1 - R)(1 + bs) + kRbs]^{-2} \{- bk (1 + bs) + Rb^2 ks (1 - k) \}] \]

\[ \text{diff equ. (14) w.r.t. 's', we have} \]

\[ \frac{d^2 t(s)}{ds^2} = b(1 - R)\{-k(1 + bs)^{-k-1}(b)\} \]

\[ = b(1 - R)(1 - R)^{-3} \{k^2 b (1 - R) + (1 - R)[-kb + bRk - bRk^2] + 2k[1 - R - 3b - Rb + kRb] \]

\[ = \frac{b}{(1-R)^2} \{kb - bR^2 k + bR^2 k^2 + k^2 b\} \]

\[ = \frac{b}{(1-R)^2} \{kb(1 - R^2) + bk^2 (1 + R^2)\} \]

\[ = \frac{b^2}{(1-R)^2} \{k(1 - R^2) + k^2 (1 + R^2)\} \]

Substituting equ. (15) in equ. (6)

\[ = \left[ \frac{\beta \lambda + \gamma c + \theta \lambda}{\beta c + \beta \lambda + \gamma c + \theta \lambda} \right] \sum_{k=1}^{\infty} \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^k \frac{b^2}{(1-R)^2} \{k(1 - R^2) + k^2 (1 + R^2)\} \]

\[ = \frac{\beta \lambda + \gamma c + \theta \lambda}{\beta c + \beta \lambda + \gamma c + \theta \lambda} \sum_{k=1}^{\infty} \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^k \frac{b^2}{(1-R)^2} \{k(1 - R^2) + k^2 (1 + R^2)\} \]

\[ = \frac{(\beta \lambda + \gamma c + \theta \lambda)b^2}{\beta c (1-R)^2} \left\{ \sum_{k=1}^{\infty} \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^k \{k(1 - R^2) + k^2 (1 + R^2)\} \right\} \]

\[ = \frac{(\beta \lambda + \gamma c + \theta \lambda)b^2}{\beta c (1-R)^2} \left\{ \sum_{k=1}^{\infty} k \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^k \right\} \]

\[ \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right] + 2 \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^2 + 3 \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^3 + \cdots \]

\[ = \frac{\beta c}{(\beta + \theta)(c + \lambda)} \left[ 1 + 2 \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right] + 3 \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^2 + \cdots \right] \]
\[
\sum_{k=1}^{\infty} k^2 \left( \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right)^k = \left( \frac{\beta c}{\beta c + \beta \lambda + \theta \lambda} \right) \left[ 1 \pm \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^{\frac{1}{2}} \left( 1 - \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right)^{\frac{3}{2}} on \ simplification
\]

\[
\sum_{k=1}^{\infty} k^2 \left[ \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^k = \left( \frac{\beta c}{\beta c + \beta \lambda + \theta \lambda} \right) \left[ 1 + \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right] \left[ 1 - \frac{\beta c}{(\beta + \theta)(c + \lambda)} \right]^{\frac{1}{3}} + (1 + R^2) \left[ \frac{\beta c [2 \beta c + \beta \lambda + \theta \lambda] [\beta c + \beta \lambda + \theta \lambda]}{\beta \lambda + \theta c + \theta \lambda} \right] \left( \beta \lambda + \theta c + \theta \lambda \right) \left( \beta \lambda + \theta c + \theta \lambda \right) \left( \beta \lambda + \theta c + \theta \lambda \right)
\]

Substituting equ. (17) and equ. (18) in equ. (16)

\[
= \frac{(\beta \lambda + \theta c + \theta \lambda) b^2}{\beta c (1 - R)^2} \left\{ (1 - R^2) \frac{\beta c [\beta c + \beta \lambda + \theta c + \theta \lambda]}{(\beta \lambda + \theta c + \theta \lambda)^2} + (1 + R^2) \frac{\beta c [2 \beta c + \beta \lambda + \theta c + \theta \lambda] [\beta c + \beta \lambda + \theta c + \theta \lambda]}{\beta \lambda + \theta c + \theta \lambda} \right\}
\]

\[
= \frac{b^2}{(1 - R)^2 (\beta \lambda + \theta c + \theta \lambda)} \left\{ (1 - R^2) (\beta c + \beta \lambda + \theta c + \theta \lambda) + (1 + R^2) \frac{\beta c [2 \beta c + \beta \lambda + \theta c + \theta \lambda] [\beta c + \beta \lambda + \theta c + \theta \lambda]}{\beta \lambda + \theta c + \theta \lambda} \right\}
\]

\[
= \frac{b^2 [\beta c + \beta \lambda + \theta c + \theta \lambda]}{(1 - R)^2 (\beta \lambda + \theta c + \theta \lambda)^2} \left\{ (1 - R^2) (\beta \lambda + \theta c + \theta \lambda) + (1 + R^2) [2 \beta c + \beta \lambda + \theta c + \theta \lambda] \right\}
\]

\[
= \frac{b^2 [\beta c + \beta \lambda + \theta c + \theta \lambda]}{(1 - R)^2 (\beta \lambda + \theta c + \theta \lambda)^2} \left\{ (1 - R^2) (\beta \lambda + \theta c + \theta \lambda) + (1 + R^2) [2 \beta c + \beta \lambda + \theta c + \theta \lambda] \right\}
\]
\[
E(T^2) = \frac{2\beta c + \beta \lambda + \theta c + \theta \lambda}{(1-R)^2(\beta \lambda + \theta c + \theta \lambda)^2} \left[ 2R^2 \beta c + 2\beta c + 2 \beta \lambda + 2 \theta c + 2\theta \lambda \right]
\]
\[
V(T) = E(T^2) - [E(T)]^2
\]
\[
V(T) = \frac{b^2[\beta c + \beta \lambda + \theta c + \theta \lambda][R^2 \beta c + \beta c + \beta \lambda + \theta c + \theta \lambda]}{(1-R)^2(\beta \lambda + \theta c + \theta \lambda)^2} - \frac{[b[\beta c + \beta \lambda + \theta c + \theta \lambda]^2}{(1-R)[\beta \lambda + \theta c + \theta \lambda]^2}
\]
\[
V(T) = \frac{b^2[\beta c + \beta \lambda + \theta c + \theta \lambda][2R^2 \beta c + 2\beta c + 2 \beta \lambda + 2 \theta c + 2\theta \lambda - \beta \lambda - \theta c - \theta \lambda]}{(1-R)^2(\beta \lambda + \theta c + \theta \lambda)^2}
\]

Table 1: Variation in E(T) and V(T) for Changes in \( \theta \) and \( \lambda = 0.5 \), \( b = 0.6 \), \( \beta = 0.5 \), \( C = 0.4 \), \( R = 0.1 \)

<table>
<thead>
<tr>
<th>( \theta )</th>
<th>E(T)</th>
<th>V(T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.8</td>
<td>0.8041</td>
<td>0.6487</td>
</tr>
<tr>
<td>1</td>
<td>0.7826</td>
<td>0.6137</td>
</tr>
<tr>
<td>1.2</td>
<td>0.7669</td>
<td>0.5896</td>
</tr>
<tr>
<td>1.4</td>
<td>0.7549</td>
<td>0.5713</td>
</tr>
<tr>
<td>1.6</td>
<td>0.7455</td>
<td>0.557</td>
</tr>
<tr>
<td>1.8</td>
<td>0.7379</td>
<td>0.5456</td>
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</table>

Fig. 1. Variation in E(T) and V(T) for Changes in \( \theta \) and \( \lambda = 0.5 \), \( b = 0.6 \), \( \beta = 0.5 \), \( C = 0.4 \), \( R = 0.1 \)
Table 2: Variation in $E(T)$ and $V(T)$ for Changes in $\lambda = 0.5$ and $\theta = 0.8$, $b = 0.6$, $\beta = 0.5$, $C = 0.4$, $R = 0.1$

<table>
<thead>
<tr>
<th>$\lambda$</th>
<th>$E(T)$</th>
<th>$V(T)$</th>
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<tbody>
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<td>1</td>
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</tr>
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<td>0.4961</td>
</tr>
<tr>
<td>3</td>
<td>0.6982</td>
<td>0.488</td>
</tr>
</tbody>
</table>

Fig. 2: Variation in $E(T)$ and $V(T)$ for Changes in $\lambda = 0.5$ and $\theta = 0.8$, $b = 0.6$, $\beta = 0.5$, $C = 0.4$, $R = 0.1$

Table 3: Variation in $E(T)$ and $V(T)$ for Changes in $\beta = 0.5$ and $C = 0.4$, $\theta = 0.8$, $\lambda = 0.5$, $R = 0.1$, $b = 0.6$

<table>
<thead>
<tr>
<th>$\beta$</th>
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<th>$V(T)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0.8041</td>
<td>0.6487</td>
</tr>
<tr>
<td>0.6</td>
<td>0.8253</td>
<td>0.6807</td>
</tr>
<tr>
<td>0.7</td>
<td>0.8411</td>
<td>0.7104</td>
</tr>
<tr>
<td>0.8</td>
<td>0.8571</td>
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</tr>
<tr>
<td>0.9</td>
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</tr>
<tr>
<td>1</td>
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</tr>
<tr>
<td>1.1</td>
<td>0.8976</td>
<td>0.8098</td>
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</table>
Fig. 3: Variation in E(T) and V(T) for Changes in $\beta = 0.5$ and $C = 0.4$, $\theta = 0.8$, $\lambda = 0.5$, $R = 0.1$, $b = 0.6$

Table 4: Variation in E(T) and V(T) for Changes in $c = 0.4$ and $\beta = 0.5$, $\theta = 0.8$, $\lambda = 0.5$, $R = 0.1$, $b = 0.6$

<table>
<thead>
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<th>$c$</th>
<th>E(T)</th>
<th>V(T)</th>
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<tbody>
<tr>
<td>0.4</td>
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<td>0.6487</td>
</tr>
<tr>
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<td>0.8253</td>
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<tr>
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<td>0.8436</td>
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<td>0.8</td>
<td>0.8733</td>
<td>0.7663</td>
</tr>
<tr>
<td>0.9</td>
<td>0.8856</td>
<td>0.7836</td>
</tr>
</tbody>
</table>

Fig. 4: Variation in E(T) and V(T) for Changes in $c = 0.4$ and $\beta = 0.5$, $\theta = 0.8$, $\lambda = 0.5$, $R = 0.1$, $b = 0.6$
Table 5: Variation in $E(T)$ and $V(T)$ for Changes in $R$ and $\beta = 0.5$, $C = 0.4$, $\theta = 0.8$, $\lambda = 0.5$, $b = 0.6$

<table>
<thead>
<tr>
<th>$R$</th>
<th>$E(T)$</th>
<th>$V(T)$</th>
</tr>
</thead>
<tbody>
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<td>0.2</td>
<td>0.9046</td>
<td>0.759</td>
</tr>
<tr>
<td>0.4</td>
<td>1.209</td>
<td>2.9923</td>
</tr>
<tr>
<td>0.6</td>
<td>1.8092</td>
<td>4.3023</td>
</tr>
<tr>
<td>0.8</td>
<td>3.618</td>
<td>18.6888</td>
</tr>
</tbody>
</table>

Fig. 5: Variation in $E(T)$ and $V(T)$ for Changes in $R$ and $\beta = 0.5$, $C = 0.4$, $\theta = 0.8$, $\lambda = 0.5$, $b = 0.6$

CONCLUSION

1. If $\theta$ which is the parameter of the random variable $Z_1$ denoting the antigenic diversity threshold increases, then $E(T)$ and $V(T)$ decreases. This is due to the fact that $Z_1$ follows exponential distribution with parameter $\theta$. So $E(T) = \frac{1}{\theta}$. As $\theta$ increases $E(Z_1)$ decreases and hence the antigenic diversity threshold is smaller. Hence it takes less time to cross the threshold. So $E(T)$ decreases, as shown in Table 1 and Fig. 1.

2. If $Z_2$ is the random variable which represents the virulence threshold is distributed as exponential with parameter $\lambda$. Then $E(Z) = \frac{1}{\lambda}$ decreases and so it takes less of time to cross the virulence threshold. Hence as $\lambda$ increases both $E(T)$ and $V(T)$ decreases, as shown in Table 2 and Fig. 2.

3. Since the random variable $X$ denoting the contribution to antigenic diversity in every contact and it is distributed as with parameter $\beta$ we have the average contribution per contact is $E(X) = \frac{1}{\beta}$. So as $\beta$ increases $E(X)$ decreases which implies the decrease in the amount of antigenic diversity contribution in each contact. Therefore, as $\beta$ increases both $E(T)$ and $V(T)$ increases, as shown in Table 3 and Fig. 3.

4. The contribution to virulence in every contact is a random variable $Y$ distributed as exponential with parameter $c$, Therefore $E(Y) = \frac{1}{c}$ which means per contact contribution to virulence on the averages. As $C$ increases there is less of contribution
to virulence. Therefore it takes longer time to cross the threshold and hence both $E(T)$ and $V(T)$ increases as $c$ increases, as shown in Table 4 and Fig. 4.

5. If the value of $R$ which represents the correlation between the inter arrival time between contacts increases, it is observed that both $E(T)$ and $V(T)$ increases as $R$ increases, as shown in Table 5 and Fig. 5.

References