CHAPTER VIII

A STOCHASTIC APPROACH TO DETERMINE TIME TO CROSS ANTIGENIC DIVERSITY THRESHOLD OF HIV TRANSMISSION USING ORDER STATISTICS

8.1 Introduction

In the study of HIV infection and consequences, the seroconversion is considered as an important aspect, since it indicates the progression of the infection leading to AIDS. In doing so, the antigenic diversity is taken to be a vital factor, since it accounts for the progression of the infection. The antigenic diversity threshold is the level beyond which the human immune system collapses. In the estimation of expected time to seroconversion, there is an important role for the interarrival times between successive contacts; and it has a significant influence.

Ratchagar et al. (2003) have derived a model for the estimation of expected time to seroconversion of HIV infected using order statistics. Kannan et al. (2008, 2009, 2011 and 2013) have obtained a stochastic model for estimation of expected time to seroconversion of HIV infected using order statistics and threshold follows Gamma, Erlang-2 and Exponentiated Exponential distribution. In this chapter, it is assumed that the threshold follows Mixed Exponential distribution and interarrival times form an order
statistics; and so they are not independent. This is due to the fact that if the smallest order statistics is taken, it implies that the interarrival times are becoming smaller. Hence frequent contacts would be possible which will have its impact on the time to seroconversion. If the largest order statistics is taken, it implies that the interarrival times are becoming larger. Hence, frequent contacts would not be possible which will have its impact on the time to seroconversion. Numerical illustrations are provided using simulated data.

8.2 Case (i) Smallest Order Statistics

8.2.1 Assumptions of the Model

- The transmission of HIV is only through sexual contacts.
- An uninfected individual has sexual contacts with HIV infected partner, and a random number of HIV are getting transmitted, at each contact.
- An individual is exposed to a damage process acting on the immune system and the damage is assumed to be linear and cumulative.
- The interarrival times between successive contacts are taken to be identically and independently distributed random variables.
- The sequence of successive contacts and threshold level are independent.
- From the collection of large number of interarrival times between successive contacts of a person, a random sample of ‘k’ observations are taken.
8.2.2 Notations

$X_i$ : a random variable denoting the increase in the antigenic diversity arising due to the HIV transmitted during the $i^{th}$ contact $X_1, X_2, \ldots, X_k$ are continuous i.i.d. random variables, with p.d.f. $g(.)$ and c.d.f. $G(.)$.

$Y$ : a random variable representing the antigenic diversity threshold which follows mixed exponential distribution with parameters($\theta_1, \theta_2$), the p.d.f being $h(.)$ and c.d.f $H(.)$.

$U_i$ : a continuous random variable denoting the inter-arrival times between the contacts follows smallest order statistics with p.d.f. $f_{u(i)}(t)$ and c.d.f. $F_{u(i)}(t)$.

$g_k(.)$ : the p.d.f of the random variable $\sum_{i=1}^{k} X_i$.

$F_k(.)$ : the $k^{th}$ convolution of $F(.)$.

$T$ : a continuous random variable denoting the time to seroconversion with p.d.f. $l(.)$ and c.d.f. $L(.)$.

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

$l^*(s)$ : the Laplace Stieltjes transform of $l(t)$.

$f^*(s)$ : the Laplace Stieltjes transform of $f(t)$.
8.2.3 Results

It can be shown that

\[ P \left[ \sum_{i=1}^{k} X_i < Y \right] = \int_{0}^{\infty} g_k(x) \bar{H}(x) \, dx \]

Let \( Y \sim \text{mixed exponential} (\theta_1, \theta_2) \)

\[ h(y) = \beta \theta_1 e^{-\theta_1 y} + (1 - \beta) \theta_2 e^{-\theta_2 y} \]

\[ H(y) = \beta \theta_1 \int_{0}^{y} e^{-\theta_1 u} \, du + (1 - \beta) \theta_2 \int_{0}^{y} e^{-\theta_2 u} \, du \]

\[ = \beta \left( 1 - e^{-\theta_1 y} \right) + (1 - \beta) \left( 1 - e^{-\theta_2 y} \right) \]

\[ \bar{H}(x) = \beta \left( e^{-\theta_1 x} - e^{-\theta_2 x} \right) + e^{-\theta_2 x} \]

Hence

\[ P \left[ \sum_{i=1}^{k} X_i < Y \right] = \beta g_k^\ast(\theta_1) + (1 - \beta) g_k^\ast(\theta_2) \]

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

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

\[ = \sum_{k=0}^{\infty} \left[ F_k(t) - F_{k+1}(t) \right] \left[ \beta g_k^\ast(\theta_1) + (1 - \beta) g_k^\ast(\theta_2) \right] \]

\( S(t) = 1 - \beta \left[ 1 - g^\ast(\theta_1) \right] \sum_{k=1}^{\infty} F_k(t) \left[ g^\ast(\theta_1) \right]^{k-1} + (1 - \beta) \left[ 1 - g^\ast(\theta_2) \right] \sum_{k=1}^{\infty} F_k(t) \left[ g^\ast(\theta_2) \right]^{k-1} \)

On simplification

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

\[ = \beta \left[ 1 - g^\ast(\theta_1) \right] \sum_{k=1}^{\infty} F_k(t) \left[ g^\ast(\theta_1) \right]^{k-1} + (1 - \beta) \left[ 1 - g^\ast(\theta_2) \right] \sum_{k=1}^{\infty} F_k(t) \left[ g^\ast(\theta_2) \right]^{k-1} \)
p.d.f of \( L(t) \) is given by
\[
l(t) = \beta \left[ 1 - g^*(\theta_1) \right] \sum_{k=1}^{\infty} f_k(t) \left[ g^*(\theta_1) \right]^{k-1} + (1 - \beta) \left[ 1 - g^*(\theta_2) \right] \sum_{k=1}^{\infty} f_k(t) \left[ g^*(\theta_2) \right]^{k-1}
\]

Now taking Laplace transform of \( l(t) \), we get
\[
l^*(s) = \frac{\beta \left[ 1 - g^*(\theta_1) \right] f^*(s)}{[1 - g^*(\theta_1)f^*(s)]} + \frac{(1 - \beta) \left[ 1 - g^*(\theta_2) \right] f^*(s)}{[1 - g^*(\theta_2)f^*(s)]}
\]

... (8.1)

The interarrival times \( U_1, U_2, U_3, \ldots, U_k \) are i.i.d random variables. Now arranging \( U_1, U_2, U_3, \ldots, U_k \) in the increasing order of magnitude we get
\[
U_{(1)} \leq U_{(2)} \leq \ldots \leq U_{(k)}.
\]

The p.d.f of the smallest order statistics is
\[
f^*_{u_{(1)}}(t) = k \left[ 1 - F(t) \right]^{k-1} f(t)
\]

Laplace transform of the same is given by
\[
f^*_{u_{(1)}}(s) = \int_0^\infty e^{-st} k \left[ 1 - F(t) \right]^{k-1} f(t) \, dt
\]

Let \( f(.) \sim \exp(\lambda) \), we can get
\[
f^*_{u_{(1)}}(s) = \frac{k\lambda}{k\lambda + s}
\]

... (8.2)

Substituting (8.2) in (8.1), we get
\[
l^*(s) = \beta \left[ 1 - g^*(\theta_1) \right] \frac{k\lambda}{k\lambda + s} + (1 - \beta) \left[ 1 - g^*(\theta_2) \right] \frac{k\lambda}{k\lambda + s}
\]

...
\[
E(T) = - \frac{d\ell^*(s)}{ds}
\]
\[
= \beta \frac{(s + k\lambda [1 - g^*(\theta_1)])(0) - [1 - g^*(\theta_1)]k\lambda}{(s + k\lambda [1 - g^*(\theta_1)])^2} \\
+ (1 - \beta) \frac{(s + k\lambda [1 - g^*(\theta_2)])(0) - [1 - g^*(\theta_2)]k\lambda}{(s + k\lambda [1 - g^*(\theta_2)])^2}
\]

at \( s = 0 \)

\[
= \beta \frac{[1 - g^*(\theta_1)]k\lambda}{(k\lambda [1 - g^*(\theta_1)])^2} + (1 - \beta) \frac{[1 - g^*(\theta_2)]k\lambda}{(k\lambda [1 - g^*(\theta_2)])^2}
\]

Let \( g^*(\theta_1) = \frac{\alpha}{\alpha + \theta_1} \), \( g^*(\theta_2) = \frac{\alpha}{\alpha + \theta_2} \)

\[
E(T) = \frac{1}{k\lambda} \left[ \frac{\beta(\alpha + \theta_1)}{\theta_1} + (1 - \beta) \frac{\alpha + \theta_2}{\theta_2} \right] \quad \text{on simplification} \quad \ldots (8.3)
\]

\[
E(T^2) = \frac{d^2\ell^*(s)}{ds^2}
\]
\[
= \frac{\beta(1 - \beta) k\lambda}{(s + k\lambda [1 - g^*(\theta_1)])^2} \\
+ \frac{\beta(1 - \beta) k\lambda}{(s + k\lambda [1 - g^*(\theta_2)])^2}
\]

at \( s = 0 \)

\[
= \frac{2k\lambda \beta [1 - g^*(\theta_1)][1 - g^*(\theta_1)]}{k\lambda^4 [1 - g^*(\theta_1)]^2} + \frac{2k\lambda (1 - \beta)[1 - g^*(\theta_2)]k\lambda [1 - g^*(\theta_2)]}{k\lambda^4 [1 - g^*(\theta_2)]^2}
\]

\[
= \frac{2k\lambda \beta \left[1 - \frac{\alpha}{\alpha + \theta_1}\right] k\lambda \left[1 - \frac{\alpha}{\alpha + \theta_1}\right]}{k\lambda^4 \left[1 - \frac{\alpha}{\alpha + \theta_1}\right]^2} + \frac{2k\lambda (1 - \beta) \left[1 - \frac{\alpha}{\alpha + \theta_2}\right] k\lambda \left[1 - \frac{\alpha}{\alpha + \theta_2}\right]}{k\lambda^4 \left[1 - \frac{\alpha}{\alpha + \theta_2}\right]^2}
\]
\[ E(T^2) = \frac{2}{(k\lambda)^2} \left[ \frac{\beta (\alpha + \theta_1)^2}{\theta_1^2} + \frac{(1-\beta)(\alpha + \theta_2)^2}{\theta_2^2} \right] \] on simplification \[ \ldots (8.4) \]

From (8.3) and (8.4), we get

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

\[ = \frac{2}{(k\lambda)^2} \left[ \frac{\beta (\alpha + \theta_1)^2}{\theta_1^2} + \frac{(1-\beta)(\alpha + \theta_2)^2}{\theta_2^2} \right] - \left\{ \frac{1}{k \lambda} \left[ \frac{\beta (\alpha + \theta_1)}{\theta_1} + \frac{(1-\beta)(\alpha + \theta_2)}{\theta_2} \right] \right\}^2 \]
8.2.4 Numerical Illustrations

Table 8.1

| k | $\alpha = 0.1$, $\beta = 0.5$, $\theta_1 = 1$, $\theta_2 - 1, \lambda = 0.1$ |
|---|---|---|
|   | E(T) | V(T) |
| 1 | 11.0000 | 121.0000 |
| 2 | 5.5000 | 30.2500 |
| 3 | 3.6667 | 13.4442 |
| 4 | 2.7500 | 7.5625 |
| 5 | 2.2000 | 4.8400 |
| 6 | 1.8333 | 3.3612 |
| 7 | 1.5714 | 2.4695 |
| 8 | 1.3750 | 1.8907 |
| 9 | 1.2222 | 1.4939 |
| 10 | 1.1000 | 1.2100 |

Figure 8.1
Table 8.2

<table>
<thead>
<tr>
<th>$\alpha$</th>
<th>$\beta = 0.5$, $\theta_1 = 1$, $\theta_2 = 1$, $\lambda = 0.5$, $k = 1$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$E(T)$</td>
</tr>
<tr>
<td>0.1</td>
<td>2.2000</td>
</tr>
<tr>
<td>0.2</td>
<td>2.4000</td>
</tr>
<tr>
<td>0.3</td>
<td>2.6000</td>
</tr>
<tr>
<td>0.4</td>
<td>2.8000</td>
</tr>
<tr>
<td>0.5</td>
<td>3.0000</td>
</tr>
<tr>
<td>0.6</td>
<td>3.2000</td>
</tr>
<tr>
<td>0.7</td>
<td>3.4000</td>
</tr>
<tr>
<td>0.8</td>
<td>3.6000</td>
</tr>
<tr>
<td>0.9</td>
<td>3.8000</td>
</tr>
<tr>
<td>1.0</td>
<td>4.0000</td>
</tr>
</tbody>
</table>

Figure 8.2
Table 8.3

<table>
<thead>
<tr>
<th>$\theta_1$</th>
<th>$\alpha = 0.1, \beta = 0.5, \theta_2 = 1, \lambda = 0.5, k = 1$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$E(T)$</td>
</tr>
<tr>
<td>0.5</td>
<td>2.3000</td>
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<tr>
<td>1.0</td>
<td>2.2000</td>
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<tr>
<td>1.5</td>
<td>2.1667</td>
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<tr>
<td>2.0</td>
<td>2.1500</td>
</tr>
<tr>
<td>2.5</td>
<td>2.1400</td>
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<tr>
<td>3.0</td>
<td>2.1333</td>
</tr>
<tr>
<td>3.5</td>
<td>2.1286</td>
</tr>
<tr>
<td>4.0</td>
<td>2.1250</td>
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<tr>
<td>4.5</td>
<td>2.1222</td>
</tr>
<tr>
<td>5.0</td>
<td>2.1200</td>
</tr>
</tbody>
</table>

Figure 8.3
Table 8.4

<table>
<thead>
<tr>
<th>$\theta_2$</th>
<th>$\alpha = 0.1, \beta = 0.5, \theta_1 = 2, \lambda = 0.5, k = 1$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$E(T)$</td>
</tr>
<tr>
<td>0.5</td>
<td>2.2500</td>
</tr>
<tr>
<td>1.0</td>
<td>2.1500</td>
</tr>
<tr>
<td>1.5</td>
<td>2.1167</td>
</tr>
<tr>
<td>2.0</td>
<td>2.1000</td>
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</tr>
<tr>
<td>5.0</td>
<td>2.0700</td>
</tr>
</tbody>
</table>

Figure 8.4
### Table 8.5

<table>
<thead>
<tr>
<th>λ</th>
<th>$\alpha = 0.1$, $\beta = 0.5$, $\theta_1 = 1$, $\theta_2 = 1$, $k = 1$</th>
<th>E(T)</th>
<th>V(T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>2.2000</td>
<td>4.8400</td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>1.1000</td>
<td>1.2100</td>
<td></td>
</tr>
<tr>
<td>1.5</td>
<td>0.7333</td>
<td>0.5379</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>0.5500</td>
<td>0.3025</td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td>0.4400</td>
<td>0.1936</td>
<td></td>
</tr>
<tr>
<td>3.0</td>
<td>0.3667</td>
<td>0.1344</td>
<td></td>
</tr>
<tr>
<td>3.5</td>
<td>0.3143</td>
<td>0.0988</td>
<td></td>
</tr>
<tr>
<td>4.0</td>
<td>0.2750</td>
<td>0.0757</td>
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</tr>
<tr>
<td>4.5</td>
<td>0.2444</td>
<td>0.0598</td>
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</tr>
<tr>
<td>5.0</td>
<td>0.2200</td>
<td>0.0484</td>
<td></td>
</tr>
</tbody>
</table>

### Figure 8.5

[Graph showing the relationship between $\lambda$ and $E(T)$ and $V(T)$]
8.2.5 Conclusions

In the case of interarrival times distributed as smallest order statistics it may be observed that:

(i) As the value of ‘k’ increases both $E(T)$ and $V(T)$ decrease. This is due to the fact that as ‘k’ namely number of contacts in $(0,t]$ increases it means that the contacts are more frequent, in other words, interarrival times between contacts become shorter. Hence it takes less time to cross the threshold. It is easily seen from the Table (8.1) and Fig. (8.1).

(ii) Parameter ‘$\alpha$’ which is the parameter of the random variables indicating the amount of contribution to the antigenic diversity increases, then it seen that both $E(T)$ as well as $V(T)$ increase as indicated in Table (8.2) and Fig. (8.2). This is due to fact that $G(.)$ follows exp $(\alpha)$, so that

$$E(X) = \frac{1}{\alpha}$$

which means that average contribution to the antigenic diversity becomes smaller as ‘$\alpha$’ increases so that $E(T)$ increases.

(iii) If $\theta_1$, which is parameter of threshold which follows mixed exponential distribution, increases then the expected time to seroconversion decreases. This is due to the fact that $E(T)$ decreases if $\theta_1$ increases. Hence the average threshold level is less; and hence it takes less time to cross the same. Hence the variance of seroconversion also decreases.
The behaviour of $E(T)$ for fixed $\alpha$, $\beta$, $\theta_1$, $k$ and $\lambda$ but with variation in $\theta_2$, is such that an increase in $\theta_2$ which is the parameter of mixed exponential of threshold increases then the expected time to seroconversion and its variance are on the decrease.

(iv) The value of both $E(T)$ and $V(T)$ decreases with an increase in $\lambda$ (Table 8.5) i.e. as the value $\lambda$ which is namely, the distribution of the interarrival times between the contacts increases, and it means that the average interarrival times between the contacts becomes smaller and thus both mean and variance of time to seroconversion decrease.
8.3 Case (ii) Largest Order Statistics

Now, the random variables $U_i$ which denote the interarrival times between contacts is taken to be the random variable $U_{(k)}$ which denotes the largest order statistics. Under the assumptions of the model case (i) which has been discussed as case (ii), the expected time to seroconversion and it’s variance are derived here under the assumption that $U_{(k)}$ denotes the largest order statistics.

The interarrival times $U_1, U_2, \ldots, U_k$ are i.i.d random variables and $U_{(1)}<U_{(2)}<\ldots<U_{(k)}$ form $k$ order statistics which are random variables that are not independent.

The p.d.f of the largest order statistics is

$$f_{u_{(k)}}(t) = k \left[ 1 - F(t) \right]^{k-1} f(t)$$

The Laplace transform of the same is given by

$$F_{u_{(k)}}(s) = \int_0^\infty e^{-st} k \left[ 1 - F(t) \right]^{k-1} f(t) \, dt$$

Assuming that $f(t)$ follows $\exp(\lambda)$. It can be shown that

$$f_{u_{(k)}}(t) = \frac{k! \lambda^k}{(\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s)} \quad \ldots (8.5)$$
Substituting (8.5) in (8.1), we get

\[
I^*(s) = \frac{\beta [1 - g^*(\theta_1)]}{1 - g^*(\theta_1)} \frac{k! \lambda^k}{(\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s)}
\]

\[
+ \frac{(1 - \beta) [1 - g^*(\theta_2)]}{1 - g^*(\theta_2)} \frac{k! \lambda^k}{(\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s)}
\]

\[
E(T) = -\frac{dI^*(s)}{ds} \bigg|_{s=0}
\]

\[
= \beta \lambda^k k! [1 - g^*(\theta_1)] \frac{d}{ds} \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_1) k! \lambda^k \right]^{-1}
\]

\[
+ (1 - \beta) \lambda^k k! [1 - g^*(\theta_2)] \frac{d}{ds} \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_2) k! \lambda^k \right]^{-1}
\]

\[
= -\beta \lambda^k k! [1 - g^*(\theta_1)] \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_1) k! \lambda^k \right]^{-2}
\]

\[
\cdot \frac{d}{ds} \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_1) k! \lambda^k \right]
\]

\[
- (1 - \beta) \lambda^k k! [1 - g^*(\theta_2)] \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_2) k! \lambda^k \right]^{-2}
\]

\[
\cdot \frac{d}{ds} \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_2) k! \lambda^k \right] \cdots (8.6)
\]

Consider \( \frac{d}{ds} \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_1) k! \lambda^k \right] \)

\[
= \left\{ (2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) + (\lambda + s)(3\lambda + s)\cdots(k\lambda + s) \right. \\
\quad + \cdots + (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k - 1)\lambda + s \right\}
\]

at \( s = 0 \)

\[
= (2\lambda,3 \lambda,4\lambda\cdots k\lambda) + (\lambda,3 \lambda,4\lambda\cdots k\lambda) + \cdots + \lambda,2\lambda,3 \lambda\cdots(k - 1)\lambda
\]
Consider \( \frac{d}{ds} \left[ \frac{\lambda + s}{\lambda + s + 1} \frac{\lambda + s + 1}{\lambda + s + 2} \cdots (k \lambda + s) - g^* (\theta_2) k! \lambda^k \right] \)

\[
= \left[ \frac{(2\lambda + s)(3\lambda + s) \cdots (k\lambda + s)}{(\lambda + s)(3\lambda + s) \cdots (k\lambda + s)} + \frac{(\lambda + s)(3\lambda + s) \cdots (k\lambda + s) + \cdots + (\lambda + s)(2\lambda + s)(3\lambda + s) \cdots (k-1)\lambda + s} \right] \\
\]

and \( s = 0 \)

\[
= \left[ (2\lambda, 3\lambda, 4\lambda \cdots k\lambda) + (\lambda, 3\lambda, 4\lambda \cdots k\lambda) + \cdots + \lambda, 2\lambda, 3\lambda \cdots (k-1)\lambda \right] \\
\]

Equation (8.6) becomes

\[
E(T) = -\beta \lambda^k k! \left[ 1 - g^* (\theta_1) \right] \left\{ \frac{(2\lambda, 3\lambda, 4\lambda \cdots k\lambda) + (\lambda, 3\lambda, 4\lambda \cdots k\lambda) + \cdots + \lambda, 2\lambda, 3\lambda \cdots (k-1)\lambda}{(\lambda, 2\lambda, 3\lambda \cdots k\lambda) - g^* (\theta_1) k! \lambda^k} \right\} \\
\]

\[
- (1 - \beta) \lambda^k k! \left[ 1 - g^* (\theta_2) \right] \left\{ \frac{(2\lambda, 3\lambda, 4\lambda \cdots k\lambda) + (\lambda, 3\lambda, 4\lambda \cdots k\lambda) + \cdots + \lambda, 2\lambda, 3\lambda \cdots (k-1)\lambda}{(\lambda, 2\lambda, 3\lambda \cdots k\lambda) - g^* (\theta_2) k! \lambda^k} \right\} \\
\]

\[
= - \beta \lambda^k k! \left[ 1 - g^* (\theta_1) \right] \prod_{m=1}^{k} m \lambda \left[ \frac{1}{\lambda} + \frac{1}{2\lambda} + \cdots + \frac{1}{k\lambda} \right] \\
\]

\[
\left[ \prod_{m=1}^{k} m \lambda - g^* (\theta_1) k! \lambda^k \right]^2 \\
\]

\[
- (1 - \beta) \lambda^k k! \left[ 1 - g^* (\theta_2) \right] \prod_{m=1}^{k} m \lambda \left[ \frac{1}{\lambda} + \frac{1}{2\lambda} + \cdots + \frac{1}{k\lambda} \right] \\
\]

\[
\left[ \prod_{m=1}^{k} m \lambda - g^* (\theta_2) k! \lambda^k \right]^2 \\
\]

\[
= - \beta \left[ 1 - g^* (\theta_1) \right] \sum_{m=1}^{k} \left( \frac{1}{m \lambda} \right) \left[ 1 - g^* (\theta_1) \right] \sum_{m=1}^{k} \left( \frac{1}{m \lambda} \right) \\
\]

\[
= - \frac{\beta}{\left[ 1 - g^* (\theta_1) \right]^2} \left[ 1 - g^* (\theta_1) \right] \sum_{m=1}^{k} \left( \frac{1}{m \lambda} \right) \\
\]

Let \( g^* (\theta_1) = \frac{\alpha}{\alpha + \theta_1}, \quad g^* (\theta_2) = \frac{\alpha}{\alpha + \theta_2} \)
\[ E(T) = \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) \left[ \frac{\beta (\alpha + \theta_1)}{\theta_1} + (1 - \beta) \frac{(\alpha + \theta_2)}{\theta_2} \right] \]

On simplification \( \quad \ldots (8.7) \)

\[ E(T^2) = \frac{d}{ds} \left[ \frac{d^2* (s)}{ds^2} \right]_{s=0} \]

\[ = -\beta \lambda^k [1 - g^*(\theta_1)] \frac{d}{ds} \left[ \frac{\left( 2\lambda+s (3\lambda+s) \cdots (k\lambda+s) \right) + \left( \lambda+s (3\lambda+s) \cdots (k\lambda+s) \right)}{\left( \lambda+s (2\lambda+s) (3\lambda+s) \cdots (k-1) \lambda+s \right)} \right] \]

\[ - (1 - \beta) \lambda^k [1 - g^*(\theta_2)] \frac{d}{ds} \left[ \frac{\left( 2\lambda+s (3\lambda+s) \cdots (k\lambda+s) \right) + \left( \lambda+s (3\lambda+s) \cdots (k\lambda+s) \right)}{\left( \lambda+s (2\lambda+s) (3\lambda+s) \cdots (k-1) \lambda+s \right)} \right] \]

\[ \quad \ldots (8.8) \]

Consider \[ \frac{d}{ds} \left[ \frac{\left( 2\lambda+s (3\lambda+s) \cdots (k\lambda+s) \right) + \left( \lambda+s (3\lambda+s) \cdots (k\lambda+s) \right)}{\left( \lambda+s (2\lambda+s) (3\lambda+s) \cdots (k-1) \lambda+s \right)} \right] \]

\[ = \left\{ \frac{\left( 2\lambda+s (3\lambda+s) \cdots (k\lambda+s) \right) + \left( \lambda+s (3\lambda+s) \cdots (k\lambda+s) \right)}{\left( \lambda+s (2\lambda+s) (3\lambda+s) \cdots (k-1) \lambda+s \right)} \right\} \]

\[ + \frac{d}{ds} \left[ \frac{\left( \lambda+s (2\lambda+s) (3\lambda+s) \cdots (k\lambda+s) \right) - g^*(\theta_1) k \lambda^k}{\left( \lambda+s (2\lambda+s) (3\lambda+s) \cdots (k\lambda+s) \right)} \right]^2 \]

\[ + \left[ \frac{\left( \lambda+s (2\lambda+s) (3\lambda+s) \cdots (k\lambda+s) \right) - g^*(\theta_1) k \lambda^k}{\left( \lambda+s (2\lambda+s) (3\lambda+s) \cdots (k\lambda+s) \right)} \right]^2 \]

\[ + \frac{d}{ds} \left[ \frac{\left( 2\lambda+s (3\lambda+s) \cdots (k\lambda+s) \right) + \left( \lambda+s (3\lambda+s) \cdots (k\lambda+s) \right)}{\left( \lambda+s (2\lambda+s) (3\lambda+s) \cdots (k-1) \lambda+s \right)} \right] \]
Consider \( \frac{d}{ds} \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_1)k!\lambda^k \right]^2 \)

\[ = -2 \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_1)k!\lambda^k \right]^3 \]

\[ \cdot \frac{d}{ds} \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_1)k!\lambda^k \right] \]

at \( s = 0 \)

\[ = -2 \left[ \frac{(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) + (\lambda + s)(3\lambda + s)\cdots(k\lambda + s) + \cdots + \lambda + s}{(\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) - g^*(\theta_1)k!\lambda^k} \right]^3 \]

\[ = \frac{2 \prod_{m=1}^{k} m\lambda \left[ 1 + \frac{1}{2\lambda} + \cdots + \frac{1}{k\lambda} \right]}{\prod_{m=1}^{k} m\lambda - g^*(\theta_1)k!\lambda^k} \]

\[ = - \frac{2 \prod_{m=1}^{k} m\lambda \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right)}{\prod_{m=1}^{k} m\lambda - g^*(\theta_1)k!\lambda^k} \]

\[ \cdots \text{(8.9)} \]

Consider \( \frac{d}{ds} \left\{ \left[ (\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k\lambda + s) \right] + \left[ (\lambda + s)(3\lambda + s)\cdots(k\lambda + s) \right] \right. \)
Consider \( \frac{d}{ds} \left[ (\lambda + s)(2\lambda + s)(3\lambda + s) \cdots (k\lambda + s) - g^* (\theta_2) k! \lambda^k \right]^{-2} \)
\[ = -2 \left[ (\lambda + s)(2\lambda + s)(3\lambda + s) \cdots (k\lambda + s) - g^* (\theta_2) k! \lambda^k \right]^{-3} \cdot \frac{d}{ds} \left[ (\lambda + s)(2\lambda + s)(3\lambda + s) \cdots (k\lambda + s) - g^* (\theta_2) k! \lambda^k \right] \]

at \( s = 0 \)
\[ = -2 \left[ (\lambda + 0.3\lambda + 0.4 \lambda \cdots k\lambda) + (\lambda + 0.3\lambda + 0.4 \lambda \cdots k\lambda) + \cdots + \lambda + 0.3\lambda \cdots (k - 1)\lambda \right] \]
\[ \left[ (\lambda + 0.2\lambda + 0.3\lambda \cdots k\lambda) - g^* (\theta_2) k! \lambda^k \right]^{-3} \]
\[ = - \frac{2 \prod_{m=1}^{k} m\lambda \left[ 1/\lambda + 1/2\lambda + \cdots + 1/k\lambda \right]}{\left[ \prod_{m=1}^{k} m\lambda - g^* (\theta_2) k! \lambda^k \right]^3} \]
\[ = - \frac{2 \prod_{m=1}^{k} m\lambda \sum_{m=1}^{k} \left( 1/m\lambda \right)}{\left[ \prod_{m=1}^{k} m\lambda - g^* (\theta_2) k! \lambda^k \right]^3} \quad \text{... (8.10)} \]

Consider \( \frac{d}{ds} \left[ (2\lambda + s)(3\lambda + s)(4\lambda + s) \cdots (k\lambda + s) \right] \bigg|_{s=0} \)
\[ = \left[ (3\lambda + s)(4\lambda + s) \cdots (k\lambda + s) \right] \frac{d}{ds} [2\lambda + s] + \left[ (2\lambda + s)(4\lambda + s) \cdots (k\lambda + s) \right] \frac{d}{ds} [3\lambda + s] \]
\[ + \cdots + \left[ (2\lambda + s)(3\lambda + s) \cdots (k - 1)\lambda + s \right] \frac{d}{ds} [k\lambda + s] \bigg|_{s=0} \]
\[ = \left[ (3\lambda + 4\lambda + 5\lambda \cdots k\lambda) + (2\lambda + 4\lambda + 5\lambda \cdots k\lambda) + \cdots + (2\lambda + 3\lambda + 5\lambda \cdots (k - 1)\lambda) \right] \]
\[ = \frac{1}{\lambda} \prod_{m=1}^{k} (m\lambda) \left[ \sum_{m=1}^{k} \left( 1/m\lambda \right) - 1/\lambda \right] \quad \text{... (8.11)} \]

Consider \( \frac{d}{ds} \left[ (\lambda + s)(3\lambda + s)(4\lambda + s) \cdots (k\lambda + s) \right] \bigg|_{s=0} \)
\[ = \frac{1}{2\lambda} \prod_{m=1}^{k} (m\lambda) \left[ \sum_{m=1}^{k} \left( 1/m\lambda \right) - 1/2\lambda \right] \quad \text{... (8.12)} \]
Consider \( \frac{d}{ds}[(\lambda + s)(2\lambda + s)(3\lambda + s)\cdots(k - 1)\lambda + s]_{s=0} \)

\[
= \frac{1}{k\lambda} \prod_{m=1}^{k} (m\lambda) \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{k\lambda} \right] \quad \cdots (8.13)
\]

Therefore equation (8.8) becomes

\[
E(T^2) = -\beta k! \lambda^k \left[ 1 - g*(\theta_1) \right] \left[ \frac{-2 \left( \prod_{m=1}^{k} m\lambda \sum_{m=1}^{k} (m\lambda) \right) \left( \prod_{m=1}^{k} m\lambda - g*(\theta_1) k! \lambda^k \right)}{\left( \prod_{m=1}^{k} m\lambda - g*(\theta_1) k! \lambda^k \right)^2} \right]
\]

\[
+ \left[ \frac{1}{k\lambda} \prod_{m=1}^{k} (m\lambda) \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{k\lambda} \right] + \frac{1}{2k\lambda} \prod_{m=1}^{k} (m\lambda) \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{2k\lambda} \right] + \cdots + \frac{1}{k!} \prod_{m=1}^{k} (m\lambda) \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{k!} \right] \right] \left( \prod_{m=1}^{k} m\lambda - g*(\theta_1) k! \lambda^k \right)^2
\]

\[
- (1 - \beta) k! \lambda^k \left[ 1 - g*(\theta_2) \right] \left[ \frac{-2 \left( \prod_{m=1}^{k} m\lambda \sum_{m=1}^{k} (m\lambda) \right) \left( \prod_{m=1}^{k} m\lambda - g*(\theta_2) k! \lambda^k \right)}{\left( \prod_{m=1}^{k} m\lambda - g*(\theta_2) k! \lambda^k \right)^2} \right]
\]

\[
+ \left[ \frac{1}{k\lambda} \prod_{m=1}^{k} (m\lambda) \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{k\lambda} \right] + \frac{1}{2k\lambda} \prod_{m=1}^{k} (m\lambda) \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{2k\lambda} \right] + \cdots + \frac{1}{k!} \prod_{m=1}^{k} (m\lambda) \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{k!} \right] \right] \left( \prod_{m=1}^{k} m\lambda - g*(\theta_2) k! \lambda^k \right)^2
\]

\[
E(T^2) = 2 \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) \right]^2 \left[ \frac{\beta (\alpha + \theta_1)^2}{\theta_1^2} + \frac{(1 - \beta)(\alpha + \theta_2)^2}{\theta_2^2} \right] + \frac{1}{\lambda} \left[ \frac{\beta (\alpha + \theta_1)}{\theta_1} + \frac{(1 - \beta)(\alpha + \theta_2)}{\theta_2} \right] \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{k\lambda} \right] \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{2k\lambda} \right] + \cdots + \frac{1}{k!} \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{k!} \right]
\]

On simplification \( \cdots (8.14) \)
From the equations (8.7) and (8.14)

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

\[ = 2 \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) \right]^2 \left[ \frac{\beta (\alpha + \theta_2)^2}{\theta_1^2} + \frac{(1 - \beta)(\alpha + \theta_2)^2}{\theta_2^2} \right] + \frac{1}{\lambda} \left[ \frac{\beta (\alpha + \theta_1)}{\theta_1} + \frac{(1 - \beta)(\alpha + \theta_2)}{\theta_2} \right] \]

\[ \left\{ \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{\lambda} \right] + \frac{1}{2} \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{2\lambda} \right] + \cdots + \frac{1}{k} \left[ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) - \frac{1}{k\lambda} \right] \right\} \]

\[ - \left\{ \sum_{m=1}^{k} \left( \frac{1}{m\lambda} \right) \left[ \frac{\beta (\alpha + \theta_1)}{\theta_1} + \frac{(1 - \beta)(\alpha + \theta_2)}{\theta_2} \right] \right\}^2 \]

On simplification
### 8.3.1 Numerical Illustrations

#### Table 8.6(a)

<table>
<thead>
<tr>
<th>k</th>
<th>(\alpha = 0.1, \beta = 0.5, \theta_1 = 1, \theta_2 = 1, \lambda = 0.1)</th>
<th>(E(T))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>11.0000</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>16.5000</td>
</tr>
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<td>3</td>
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<tr>
<td>4</td>
<td></td>
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<tr>
<td>5</td>
<td></td>
<td>25.1167</td>
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<tr>
<td>6</td>
<td></td>
<td>26.9500</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>28.5214</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>29.8964</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>31.1187</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>32.2187</td>
</tr>
</tbody>
</table>

#### Table 8.6(b)

<table>
<thead>
<tr>
<th>k</th>
<th>(\alpha = 0.1, \beta = 0.5, \theta_1 = 1, \theta_2 = 1, \lambda = 0.1)</th>
<th>(V(T))</th>
</tr>
</thead>
<tbody>
<tr>
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<td>2</td>
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<td>7</td>
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<td>2524.7576</td>
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<tr>
<td>10</td>
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<td>3937.7200</td>
</tr>
</tbody>
</table>

#### Figure 8.6(a)

![Plot of E(T) vs. k](image)

#### Figure 8.6(b)

![Plot of V(T) vs. k](image)
Table 8.7

<table>
<thead>
<tr>
<th>$\alpha$</th>
<th>$\beta = 0.5$, $\theta_1 = 1$, $\theta_2 = 1$, $\lambda = 0.5$, $k = 8$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$E(T)$</td>
</tr>
<tr>
<td>0.1</td>
<td>5.9793</td>
</tr>
<tr>
<td>0.2</td>
<td>6.5229</td>
</tr>
<tr>
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<td>9.2407</td>
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<td>9.7843</td>
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<tr>
<td>0.9</td>
<td>10.3279</td>
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<td>1.0</td>
<td>10.8714</td>
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</table>

Figure 8.7
Table 8.8

<table>
<thead>
<tr>
<th>$\theta_1$</th>
<th>$\alpha = 0.1$, $\beta = 0.5$, $\theta_2 = 1$, $\lambda = 0.5$, $k = 8$</th>
</tr>
</thead>
<tbody>
<tr>
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<td>$E(T)$</td>
</tr>
<tr>
<td>0.5</td>
<td>6.2511</td>
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Figure 8.8
Table 8.9

<table>
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<tr>
<th>$\theta_2$</th>
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<td>V(T)</td>
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</tr>
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<td>5.8434</td>
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</table>

Figure 8.9
Table 8.10

<table>
<thead>
<tr>
<th>$\lambda$</th>
<th>$\alpha = 0.1, \beta = 0.5, \theta_1 = 1, \theta_2 = 1, k = 8$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$E(T)$</td>
</tr>
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<td>0.5</td>
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Figure 8.10
8.3.2 Conclusions

In the case of interarrival times distributed as largest order statistics, the following observations can be made.

(i) The value of both \( E(T) \) and \( V(T) \) increases with an increase in ‘\( k \)’ (Table 8.6(a) and 8.6(b)) namely the number of contacts. If ‘\( k \)’ becomes larger then the corresponding \( U_{(k)} \) the mean and variance of time to seroconversion also become larger thereby implying that it is the largest of the interarrival times in such a case the inter contact times are elongated thereby having a delayed time to seroconversion.

(ii) As the value of ‘\( \alpha \)’ which is namely the parameter of the random variable \( X_i \) denoting contribution to the antigenic diversity increase then it is seen that mean time to seroconversion and variance time to seroconversion increase as indicated in Table 8.7.

(iii) If \( \theta_1 \), which is parameter of threshold which follows mixed exponential distribution, increases then the expected time to seroconversion decreases. This is due to the fact that \( E(T) \) decreases if \( \theta_1 \) increases. Hence the average threshold level is less; and hence it takes less time to cross the same. Hence the variance of seroconversion also decreases.

The behaviour of \( E(T) \) for fixed \( \alpha, \beta, \theta_1, k \) and \( \lambda \) but with variation in \( \theta_2 \), is such that an increase in \( \theta_2 \) which is the parameter of mixed
exponential of threshold increases then the expected time to seroconversion and its variance are on the decrease.

(iv) As the value of parameter of \( \lambda \) which is namely parameter of the distribution of the interarrival times between the contacts increase it means that the average interarrival times which is given by \( E(U) = \frac{1}{\lambda} \), since \( U \) follows \( \text{exp}(\lambda) \). Therefore interarrival times between the contacts become smaller and hence the mean and variance of the time to seroconversion also decrease.