ABSTRACT

This study has proposed a stochastic model for cancerous growth due to its metastasis in an organ. Birth, Death and Migration processes based on growth and loss rates of mutant and normal cells are considered. It is assumed that the growth and loss rates of both normal and mutant cells follow Poisson processes. The joint probability generating functions along with statistical measures were derived. Model behaviour was analysed with a numerical data.

KEYWORDS: Stochastic Modelling, Birth and Death Processes, Differential equations, Cancer cell growth.

1. INTRODUCTION

Human body is a collection of different type of cells and tissues. They are in the different structure in the growth, generation and loss. Cell division in the organ is regulated by genetic instruction of the body and the mechanism of alleles in the gene. The prime cause of cancer problem may be due to improper cell division and its irregular proliferation. Continuous proliferation with minimum rate of death in mutant cells will form an accumulation of corrupted cells called tumour. The Process of mitosis includes either normal cell may produce two normal cells or a normal cell may produce one normal and one mutant cell. Once a normal cell is transformed as mutant cell, it will further produce mutant cells only. The blood circulation system in the body makes the invasion of cancer cells to the adjacent parts from the site of its generation.

The growth of solid tumours are influenced by their physical characteristics and factors related to tumour growth are random and dependent \(^{[1]}\). The growth of carcinogenesis is age
dependent and stochastic in nature\cite{2}. The growth of a tumor is stochastic and density dependent branching process follows diffusion approximations of continuous time \cite{3}. Carcinogenesis with time dependent parameters is a two stage and stochastic formulated from the adult tumours\cite{4}. Formation of metastatic foci at distant sites in a human body is purely stochastic and can be estimated through modeling\cite{5}. The growth of cancer cell with respect to spontaneous mutation and proliferation shall be happened when the proliferation and death processes of both mutant and normal cells are Poisson. Further they are stochastic and density dependent with heterogeneous growth/loss rates of mutant/normal cells\cite{6}. The cancer cell growth is stochastic and two staged when the growth/loss of pre malignant, malignant cells are Poisson parameters\cite{7}.

The model behind metastasis progression of cancer cell is completely mechanistic and stochastic having exponential growth for primary and secondary tumours\cite{8}. Tumour growth is according to Gompertz law when cell division and cell death are the density functions of the size of tumour under uncertainty conditions\cite{9}. Stochastic and hierarchical modelling is observed in the formation with cancerous stem cells and its metastatic progression\cite{10}. Formation of cancer metastases via cancer stem cells is modeled with the assumptions under stochasticity conditions\cite{11}. The joint probability function of malignant cells is based on a bivariate time dependent Poisson process for getting two stage stochastic modeling in cancer growth from normal to malignant cells\cite{12}. Multistage malignant tumor with non-homogeneous Poisson process is modeled with continuous time stochasticity\cite{13}. Treatment dependent malignancy growth and the uncertainty issues are the dependent factors for modeling the cancer growth\cite{14}.

The growth of mutant cells in an organ has fluctuating rates due to the random phenomena in the division of cells. The growth rate of mutant cells is irregular and faster than normal cells. This study develops a bivariate stochastic model for quantifying the size of normal and cancer cells in an organ. The reproduction and mortality rates of normal cells, mutant cells, transformation and migrations rates of mutant cells assumed to follow Poisson processes. The following schematic diagram will explain the processes of cancer formation and its spread to different organ in a body.
2. STOCHASTIC MODEL FOR GROWTH OF CANCEROUS CELL

The mechanisms involved in the cell divisions are purely stochastic in nature. Let the events occurred in non-overlapping interval of time are statistically independent. Let $\Delta t$ be an infinitesimal interval in the time.

Let $\lambda_{ij}$ be the growth rate of $i^{th}$ stage cells in $j^{th}$ stage tumor; $\mu_{ij}$ be the loss rate of $i^{th}$ stage cells in $j^{th}$ stage tumor; $\delta_{ij}$ be the transformation rate of $i^{th}$ stage cells to $(i+1)^{th}$ stage in the $j^{th}$ stage tumor to $(j+1)^{th}$ stage of tumor.

Where,

$i=1,2,3$: Normal stage of cell, Mutant stage of cell, Migrant mutant stage of cell.

$j=1,2$: Primary tumor, Secondary tumor.

Let $\{N(t), t \geq 0\}$ be the process of normal cell division (growth/loss) and $\{M(t), t \geq 0\}$ be the process of mutant cell division (growth/loss). Let $\{N(t),M(t), t \geq 0\}$ be a joint bivariate stochastic processes of individual stochastic processes of $\{N(t), t \geq 0\}$ and $\{M(t), t \geq 0\}$. Such that, $\Pr\{(N(t), M(t)) = (n, m)\} = P_{n,m}(t)$ and marginal processes are $\Pr\{N(t) = n\} = P_n(t), \Pr\{M(t) = m\} = P_m(t)$.

Further,

$\Pr\{N(\Delta t) = u / N(t) = n\} = P_{nu}$ for $u = n + 1, n - 1, n, n \pm 2$

$\Pr\{M(\Delta t) = v / M(t) = m\} = P_{mv}$ for $v = m + 1, m - 1, m, m \pm 2$

$\Pr\{[(N(\Delta t), M(\Delta t)) = (u, v)] / [(N(t), M(t)) = (n, m)]\} = P_{nu,mv}$ for $v = m + 1, m - 1, m, m \pm 2$
Let us now define postulates of the univariate process with respect to normal and mutant growth,

\[ P_{n,u} = P\{N(\Delta t) = u/N(t) = n\} \]
\[ = n\lambda_{11}\Delta t + o(\Delta t); u = n + 1 \]
\[ = n\mu_{11}\Delta t + o(\Delta t); u = n - 1 \]
\[ = n\delta_{11}\Delta t + o(\Delta t); u = n - 1 \]
\[ = 1 - \{n(\lambda_{11} + \mu_{11} + \delta_{11})\Delta t + o(\Delta t)\}; u = n \]
\[ = o(\Delta t)^2; u = n \pm 2 \]

For mutant growth processes,

\[ P_{m,v} = P\{M(\Delta t) = v/M(t) = m\} \]
\[ = m\lambda_{21}\Delta t + o(\Delta t); v = m + 1 \]
\[ = m\mu_{21}\Delta t + o(\Delta t); v = m - 1 \]
\[ = m\delta_{21}\Delta t + o(\Delta t); v = m - 1 \]
\[ = n(\lambda_{32} + \mu_{32} + \delta_{32})\Delta t + o(\Delta t); v = m \]
\[ = o(\Delta t)^2; v = m \pm 2 \]

Considering the joint stochastic processes, we have

\[ P_{nu,mv} = P\{(N(\Delta t), M(\Delta t)) = (u, v)\}/(N(t), M(t) = (n, m)) \]
\[ = n\lambda_{21}\Delta t + o(\Delta t); u = n + 1, v = m \]
\[ = n\mu_{21}\Delta t + o(\Delta t); u = n - 1, v = m \]
\[ = n\delta_{21}\Delta t + o(\Delta t); u = n - 1, v = m \]
\[ = m\lambda_{21}\Delta t + o(\Delta t); u = n, v = m + 1 \]
\[ = m\mu_{21}\Delta t + o(\Delta t); u = n, v = m - 1 \]
\[ = m\delta_{21}\Delta t + o(\Delta t); u = n, v = m - 1 \]
\[ = n(\lambda_{32} + \mu_{32} + \delta_{32})\Delta t + o(\Delta t); u = n, v = m - 1 \]
\[ = o(\Delta t)^2; u = n, v = m \pm 2 \]

Let \( P_{n,m}(t + \Delta t) \) be the probability that happening of an event of one event in an infinitesimal interval \( \Delta t \), there exists ‘n’ normal and ‘m’ mutant cells in the organ upto time ‘t’. Then the differential - difference equations of the model are:
\[ P_{n,m}(t) = -\{n(\lambda_{11} + \delta_{11} + \mu_{11}) + m(\lambda_{21} + \mu_{21} + \delta_{21}) + (\lambda_{32} + \mu_{32} + \delta_{32})\}P_{n,m}(t) \\
+ (n-1)\lambda_{n-1,m}P_{n-1,m-1}(t) + (n+1)\delta_{11,n+1,m-1}(t) + (m-1)\lambda_{n+1,m-1}P_{n,m-1}(t) + (m+1)\mu_{11}P_{n+1,m-1}(t) \\
+ [(m+1)(\mu_{21} + \delta_{21}) + \mu_{32} + \delta_{32}]P_{n+1,m-1}(t) + \lambda_{32}P_{n,m-1}(t) \quad \text{for } n, m \geq 1 \quad (2.1) \]

\[ P_{0,1}(t) = -[\lambda_{21} + \lambda_{32} + \mu_{21} + \mu_{32} + \delta_{21}]P_{0,1}(t) + \mu_{11}P_{1,1}(t) + \delta_{11}P_{1,0}(t) \\
+ [2(\mu_{21} + \delta_{21}) + \mu_{32} + \delta_{32}]P_{0,2}(t) + \lambda_{32}P_{0,0}(t) \quad (2.2) \]

\[ P_{1,0}(t) = -(\lambda_{11} + \delta_{11} + \lambda_{32} + \mu_{11} + \delta_{21} + \mu_{32} + \delta_{32})P_{0,0}(t) + 2\mu_{11}P_{2,0}(t) \\
+ (\mu_{11} + \delta_{21} + \mu_{32} + \delta_{32})P_{1,1}(t) \quad (2.3) \]

\[ P_{0,0}(t) = -(\lambda_{32} + \mu_{32} + \delta_{32})P_{0,0}(t) + \mu_{11}P_{1,0}(t) + (\mu_{11} + \delta_{21} + \mu_{32} + \delta_{32})P_{0,1}(t) \quad (2.4) \]

With the initial condition
\[ P_{N_0,M_0}(t) = 1, P_{i,j}(0) = 0 \quad \forall i \neq N_0; j \neq M_0 \]

3. GENERATING FUNCTIONS AND STATISTICAL MEASURES

Let \( P(x,y;t) \) be the probability generating function of \( P_{n,m}(t) \).

Where, \( P(x,y;t) = \sum_{n=0}^{\infty} \sum_{m=0}^{\infty} x^n y^m P_{n,m}(t) ; |x| < 1, |y| < 1 \). Multiplying the above differential-difference equations from Eqs. (2.1) to (2.4) with \( x^n y^m \) and summing over \( n, m \), we get

\[ \frac{\partial}{\partial t} P(x,y;t) = -\{\lambda_{11} + \delta_{11} + \mu_{11}\} \sum_{m=0}^{\infty} \sum_{n=0}^{\infty} nx^n y^m P_{n,m}(t) - (\lambda_{21} + \mu_{21} + \delta_{21}) \sum_{m=0}^{\infty} \sum_{n=0}^{\infty} mx^n y^m P_{n,m}(t) \\
- (\lambda_{32} + \mu_{32} + \delta_{32}) \sum_{m=0}^{\infty} \sum_{n=0}^{\infty} x^n y^m P_{n,m}(t) + \lambda_{11} \sum_{m=0}^{\infty} \sum_{n=0}^{\infty} (n-1)x^n y^m P_{n-1,m}(t) \\
+ \delta_{11} \sum_{m=0}^{\infty} \sum_{n=0}^{\infty} (n+1)x^n y^m P_{n+1,m}(t) + \lambda_{21} \sum_{m=0}^{\infty} \sum_{n=0}^{\infty} (m-1)x^n y^m P_{n,m-1}(t) \\
+ \mu_{11} \sum_{m=0}^{\infty} \sum_{n=0}^{\infty} (n+1)x^n y^m P_{n+1,m}(t) + (\mu_{21} + \delta_{21}) \sum_{m=0}^{\infty} \sum_{n=0}^{\infty} (m+1)x^n y^m P_{n,m+1}(t) \\
+ [\mu_{32} + \delta_{32}] \sum_{m=0}^{\infty} \sum_{n=0}^{\infty} x^n y^m P_{n,m+1}(t) + \lambda_{32} \sum_{m=0}^{\infty} \sum_{n=0}^{\infty} x^n y^m P_{n,m-1}(t) \quad (3.1) \]

On simplification we obtain,
\[
\frac{\partial}{\partial t} P(x, y; t) = \{-(\lambda_{11} + \delta_{11} + \mu_{11})x + \mu_{11} + \lambda_{11}x^2 + \delta_{11}y\} \frac{\partial}{\partial x} P(x, y; t) + \{-(\lambda_{21} + \mu_{21} + \delta_{21})y + \lambda_{21}y^2 + (\mu_{21} + \delta_{21})\} \frac{\partial}{\partial y} P(x, y; t) + \{-(\lambda_{32} + \mu_{32} + \delta_{32}) + \frac{[\mu_{32} + \delta_{32}]}{y} + \lambda_{32}y\} P(x, y; t)
\]

(3.2)

We can obtain the characteristics of the model using joint cumulant generating function of \(P_{n,m}(t)\). Taking \(x = e^u\), \(y = e^v\) and denoting \(k(u, v; t)\) as the joint cumulant generating function of \(P_{n,m}(t)\) we get the following expression

\[
\frac{\partial}{\partial t} k(u, v; t) = \{-(\lambda_{11} + \delta_{11} + \mu_{11}) + \lambda_{11}e^u + \delta_{11}e^v\} \frac{\partial}{\partial u} k(u, v; t) + \{-(\lambda_{21} + \mu_{21} + \delta_{21}) + \lambda_{21}e^v\} \frac{\partial}{\partial v} k(u, v; t) + \{-(\lambda_{32} + \mu_{32} + \delta_{32}) + \frac{[\mu_{32} + \delta_{32}]}{e^v} + \lambda_{32}e^v\} k(u, v; t)
\]

(3.3)

Comparing the coefficient of the power of \(u\)'s in the above equations, we get the following

\[
\frac{\partial}{\partial t} m_{1,0}(t) = (\lambda_{11} - \delta_{11} - \mu_{11}) m_{1,0}(t)
\]

(3.4)

\[
\frac{\partial}{\partial t} m_{0,1}(t) = \delta_{11}m_{1,0}(t) + (\lambda_{21} - \mu_{21} - \delta_{21})m_{0,1}(t)
\]

(3.5)

\[
\frac{\partial}{\partial t} m_{2,0}(t) = 2(\lambda_{11} - \delta_{11} - \mu_{11})m_{2,0}(t) + (\lambda_{11} + \delta_{11} + \mu_{11})m_{1,0}(t)
\]

(3.6)

\[
\frac{\partial}{\partial t} m_{0,2}(t) = \delta_{11}m_{1,0}(t) + (\lambda_{21} + \mu_{21} + \delta_{21})m_{0,1}(t) + 2(\lambda_{32} - \mu_{21} - \delta_{32})m_{0,2}(t) + 2(\lambda_{32} - \mu_{32} - \delta_{32})m_{0,1}(t) + \delta_{11}m_{1,1}(t)
\]

(3.7)

\[
\frac{\partial}{\partial t} m_{1,1}(t) = (\lambda_{11} - \delta_{11} - \mu_{11})m_{1,1}(t) + \delta_{11}m_{2,0}(t) - \delta_{11}m_{1,0}(t) + (\lambda_{21} - \mu_{21} - \delta_{21})m_{1,1}(t) + (\lambda_{21} - \mu_{21} - \delta_{21})m_{1,1}(t) + \delta_{11}m_{2,0}(t)
\]

(3.8)

Let \(m_{i,j}(t)\) denotes the moments of order \((i,j)\) of the normal cells, mutant cells in an organ at time \(t\). Then the characteristics of the model are obtained by solving the above ordinary linear differential equations, which are as follows

Expected number of normal cells in an organ at time ‘\(t\)’
\[ m_{1,0}(t) = N_0 e^{At} \]  
(3.9)

Expected number of mutant cells in an organ at time ‘t’
\[ m_{0,1}(t) = \frac{\delta_{11}N_0 e^{At}}{A-B} + \left( M_0 - \frac{\delta_{11}N_0}{A-B} \right) e^{Bt} \]  
(3.10)

Variance of number of normal cells in the organ at time ‘t’
\[ m_{2,0}(t) = \frac{DN_0 e^{At}}{A} (e^{At} - 1) \]  
(3.11)

Variance of number of mutant cells in the organ at time ‘t’
\[ m_{0,2}(t) = \frac{\delta_{11}N_0 e^{At}}{A-2B} + (F + 2E) \left\{ \frac{\delta_{11}N_0 e^{At}}{(A-2B)(A-B)} - \left( M_0 - \frac{\delta_{11}N_0}{A-B} \right) \frac{e^{Bt}}{B} \right\} + \delta_{11} \left\{ \frac{\delta_{11}N_0 D}{A} \left( \frac{e^{2At}}{2(A-B)^2} + \frac{e^{At}}{(A-2B)B} \right) - \frac{(E-\delta_{11})N_0 e^{At}}{(A-2B)B} \right\} \right\} \]  
(3.12)

Covariance of number of normal and mutant cells in an organ at time ‘t’
\[ m_{1,1}(t) = \left\{ \frac{(E-\delta_{11})N_0 e^{-Bt}}{-B} + \delta_{11} \frac{DN_0}{A} \left( \frac{e^{2At}}{(A-B)} + \frac{e^{At}}{B} \right) \right\} + \left\{ \frac{\delta_{11}DN_0 - (A-B)(E-\delta_{11})N_0}{(A-B)B} \right\} e^{(A+B)t} \]  
(3.13)

Where, \( N_0 \) \& \( M_0 \) - Initial number of normal and mutant cells in an organ.
\[ A = \lambda_{11} - \delta_{11} - \mu_{11} \quad B = \lambda_{21} - \mu_{21} - \delta_{21} \quad D = \lambda_{11} + \delta_{11} + \mu_{11} \quad E = \lambda_{32} - \mu_{32} - \delta_{32} \quad F = \lambda_{21} + \mu_{21} + \delta_{21} \]
4. NUMERICAL ILLUSTRATION

The computed values of the characteristics of the model \( m_{1,0}(t), m_{0,1}(t), m_{2,0}(t), m_{0,2}(t) \) and \( m_{1,1}(t) \) mentioned above from Eqs. (3.9) to (3.13) for the parameters are presented in the table for changing values of \( \lambda_{11}, \delta_{11}, \lambda_{21}, \lambda_{32}, \mu_{11}, \mu_{21}, \delta_{21}, \mu_{32}, \delta_{32}, N_0, M_0 \) and time \( t \) in the appendix-1. The pictorial representation of changing patterns of statistical measures with respect to the study parameters are in appendix-2.

5. FINDINGS

The findings were made by varying a single parameter and keeping other parameters are constant.

- \( m_{1,0}, m_{0,1}, m_{2,0}, \) and \( m_{0,2} \) are increasing functions and, \( m_{1,1} \) is negative and increasing function of \( \lambda_{11}. \)
- \( m_{1,0}, m_{2,0}, m_{0,2} \) are the decreasing functions, \( m_{0,1} \) is increasing function and \( m_{1,1} \) is negative and increasing function \( \delta_{11}. \)
- \( m_{1,0}, m_{2,0} \) are invariant, \( m_{0,1}, m_{0,2} \) are increasing function and \( m_{1,1} \) is negative and decreasing function of \( \lambda_{21}. \)
- \( m_{1,0}, m_{0,1} \) and \( m_{2,0} \) are invariant, \( m_{0,2} \) is decreasing function and \( m_{1,1} \) is negative and increasing function of \( \lambda_{32}. \)
- \( m_{1,0}, m_{0,1}, m_{2,0}, \) and \( m_{0,2} \) are decreasing functions and \( m_{1,1} \) is negative and increasing function of \( \mu_{11}. \)
- \( m_{1,0}, m_{2,0} \) are invariant \( m_{0,1}, m_{0,2} \) are decreasing functions and \( m_{1,1} \) is negative and increasing function of \( \mu_{21}. \)
- \( m_{1,0}, m_{2,0} \) are invariant and \( m_{0,1}, m_{0,2} \) are decreasing functions and \( m_{1,1} \) is negative and increasing function of \( \delta_{21}. \)
- \( m_{1,0}, m_{0,1} \) and \( m_{2,0} \) are invariant, \( m_{0,2} \) is increasing function and \( m_{1,1} \) is negative and decreasing function of \( \mu_{4}. \)
- \( m_{1,0}, m_{0,1}, \) and \( m_{2,0} \) is invariant, \( m_{0,2} \) is increasing function and \( m_{1,1} \) is negative and decreasing function of \( \mu_{5}. \)
- \( m_{1,0}, m_{0,1}, m_{2,0}, \) and \( m_{0,2} \) are increasing functions and \( m_{1,1} \) is negative and decreasing function of \( N_0. \)
- \( m_{1,0}, m_{2,0} \) are invariant, \( m_{0,1} \) is increasing function, \( m_{0,2} \) is decreasing function and \( m_{1,1} \) is negative and invariant of \( M_0. \)
- $m_{1,0}$, $m_{2,0}$ are decreasing function, $m_{0,1}$, $m_{0,2}$ are increasing function and $m_{1,1}$ is negative and decreasing function of $t$.

**ACKNOWLEDGEMENTS**

The authors are thankful to acknowledge the funding agency to extract this study as the first author is the principal investigator of a major research project work entitled “Studies on Stochastic Models for Cancer Growth and its Applications with Optimal Drug Administration in Chemotherapy” sponsored by the Scientific and Engineering Research Board (SERB), Department of Science and Technology (DST), Govt. of India.

**REFERENCES**

**Appendix-1:** Table for all statistical measures with varying values of one parameter when other parameters are fixed

<table>
<thead>
<tr>
<th>$\lambda_1$</th>
<th>$\lambda_2$</th>
<th>$\lambda_3$</th>
<th>$\mu_3$</th>
<th>$\mu_4$</th>
<th>$\mu_5$</th>
<th>$N_0$</th>
<th>$M_0$</th>
<th>$t$</th>
<th>$m_{00}$</th>
<th>$m_{20}$</th>
<th>$m_{02}$</th>
<th>$m_{11}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
<td>0.01</td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
</tr>
<tr>
<td>1.1</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
<td>0.01</td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>49.319</td>
</tr>
<tr>
<td>1.2</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
<td>0.01</td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>54.506</td>
</tr>
<tr>
<td>1.3</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
<td>0.01</td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>60.239</td>
</tr>
<tr>
<td>1.4</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
<td>0.01</td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>66.574</td>
</tr>
<tr>
<td>1.5</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
<td>0.01</td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>73.01</td>
</tr>
<tr>
<td>1.6</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
<td>0.01</td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>79.643</td>
</tr>
</tbody>
</table>

www.jiarm.com
Appendix-1: Table for all statistical measures with varying values of one parameter when other parameters are fixed

<table>
<thead>
<tr>
<th>$\lambda_1$</th>
<th>$\lambda_2$</th>
<th>$\lambda_3$</th>
<th>$\lambda_4$</th>
<th>$\mu_1$</th>
<th>$\mu_2$</th>
<th>$\mu_3$</th>
<th>$\mu_4$</th>
<th>$\mu_5$</th>
<th>$N_0$</th>
<th>$M_0$</th>
<th>$t$</th>
<th>$m_{10}$</th>
<th>$m_{01}$</th>
<th>$m_{20}$</th>
<th>$m_{02}$</th>
<th>$m_{11}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>10510</td>
<td>80.893</td>
<td>2190</td>
<td>-144.235</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>10310</td>
<td>80.893</td>
<td>1753</td>
<td>-141.005</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>10110</td>
<td>80.893</td>
<td>1333</td>
<td>-137.728</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9921</td>
<td>80.893</td>
<td>929.13</td>
<td>-134.728</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>604.165</td>
<td>-156.295</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>572.753</td>
<td>-143.987</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>547.623</td>
<td>-134.140</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>529.408</td>
<td>-134.532</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>502.182</td>
<td>-133.384</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>474.956</td>
<td>-128.285</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>447.728</td>
<td>-122.626</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>420.500</td>
<td>-116.528</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>393.272</td>
<td>-110.432</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>366.044</td>
<td>-104.332</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>338.816</td>
<td>-98.232</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>311.588</td>
<td>-92.132</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>284.359</td>
<td>-86.032</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>257.130</td>
<td>-79.932</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>230.901</td>
<td>-73.832</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>204.672</td>
<td>-67.732</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>178.443</td>
<td>-61.632</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>152.214</td>
<td>-55.532</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>126.985</td>
<td>-49.432</td>
</tr>
<tr>
<td>1.0</td>
<td>2.0</td>
<td>4.0</td>
<td>0.1</td>
<td>0.5</td>
<td>0.1</td>
<td>0.1</td>
<td>0.01</td>
<td></td>
<td>200</td>
<td>500</td>
<td>1</td>
<td>44.626</td>
<td>9731</td>
<td>80.893</td>
<td>101.756</td>
<td>-43.332</td>
</tr>
</tbody>
</table>

www.jiarm.com
Appendix-2: figures for different statistical measures with varying values of one parameter when other parameters are fixed