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TRIVARIATE STOCHASTIC MODELING FOR TUMOR CELL GROWTH USING SECOND ORDER MOMENTS IN THE PRESENCE OF ONCOLYTIC VIROTHERAPY

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Abstract

In this review, a stochastic model is made for assessing the immediate impact of viral implantation on cancer cell improvement. The Second order moments of the cells were assessed utilizing a trivariate Probability work got from the distinction differential conditions. This assessment model may help with the improvement of another healing for oncolytic virotherapy.

Introduction

Malignancy is a conventional term for an enormous gathering of infections that can influence any piece of the body. Different terms utilized are dangerous cancers and neoplasms. One characterizing component of disease is the rapid production of strange cells that develop past their typical limits, and which would then be able to attack abutting portions of the body and spread to different organs; the last cycle is alluded to as metastasis.

Cancer emerges from the change of ordinary cells into tumor cells in a

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multi-stage process that for the most part advances from a pre-carcinogenic sore to a dangerous cancer. These progressions are the after effect of the association between an individual's hereditary components.

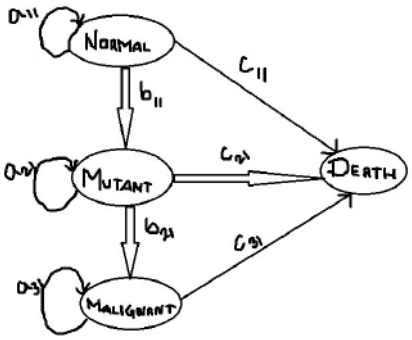
The new presentation of viruses as a weapon against cancer can be viewed as one of the most interesting methodologies with regards to accuracy medication. The job of resistant designated spot inhibitors has been widely contemplated in ahead of schedule and progressed malignant growth stages, with unprecedented outcomes. In spite of the fact that there is a decent bearableness profile, particularly when contrasted and customary chemotherapy, extreme insusceptible related unfriendly occasions have arisen as a possible restriction. Also, there are still treatment-safe cases and subsequently further treatment choices should be executed.

In the paper of P. T. Rao, K. Madhavi and S. K. Masthan Babu [4] (2011), they have made stochastic model for freak cell headway under chemotheraphy with the suspicion that the effect of medication has specific sensibility scales and essentially stochastic taking into account different records. The comparative question is reached the Normal, Mutant and Malignant cells under the presence of OV. A Trivariate stochastic Model for the headway of development cell under the presence of viral treatment is made utilizing the second order moments and the impact on the malignant growth cell inside seeing the viral implantation is investigated.

Assumptions of the Stochastic Model

The following assumptions are considered to develop the stochastic model. Let us suppose that the trials considered without overlapping be statistically independent. Let be an infinitesimal interval of time.

At time τ, suppose there are 'η' normal cells, 'μ' mutant cells, and 'λ' malignant cells. Let $a_{\alpha\beta}$ be the growth rate, $b_{\beta\gamma}$ be the speed with which cells convert from γ to $\gamma + 1$ stage, $c_{\alpha\beta}$ be the death rate of cells, where 'a' be the stage of cells, $\alpha = 1, 2, 3$ for normal, mutant, malignant cells respectively, '$\beta = 1$' be the presence of the viral injection and 'γ' be the cell transformation from γ to $\gamma + 1$ stage, $\gamma = 1, 2$.



Stochastic Model.

Assume that all of the above occurrences are governed by the Poisson Process.

Analysis of the Model

Let $\{P(\tau), \tau \geq 0\}, \{Q(\tau), \tau \geq 0\}\{R(\tau), \tau \geq 0\}$ be the individual stochastic processes of Normal cells, Mutant cells and Malignant cells such that $P\{P(\tau) = \eta\} = P_n(\tau)$, $P\{Q(\tau) = \mu\} = P_\mu(\tau)$ and $P\{P(\tau) = \lambda\} = P_\lambda(\tau)$ and the joint process will be $P\{P(\tau), Q(\tau), R(\tau) = (\eta, \mu, \lambda)\} = P_{\eta, \mu, \lambda}(\tau)$.

In the presence of viral injection, the likelihood of production of one normal cell to another normal cell, the likelihood of production of one normal cell to one mutant cell, the likelihood of production of one mutant cell to another mutant cell, the likelihood of production of one mutant cell to one malignant cell, the likelihood of production of one malignant cell to another malignant cell at the time be

$$\eta a_{11}\Delta\tau + o(\Delta\tau),\ \eta b_{11}\Delta\tau + o(\Delta\tau),$$

$$\mu a_{21}\Delta\tau + o(\Delta\tau),\ \mu b_{21}\Delta\tau + o(\Delta\tau),$$

$$\lambda a_{31}\Delta\tau + o(\Delta\tau)$$

respectively.

One normal cell's probability of dying is $\eta c_{11}\Delta\tau + o(\Delta\tau)$

One mutant cell's probability of dying is $\mu c_{21}\Delta\tau + o(\Delta\tau)$

One malignant cell's probability of dying is $\lambda c_{31}\Delta\tau + o(\Delta\tau)$.

Probability of no generation of normal cell to normal cell, from normal to mutant, from normal cell to malignant cell, from mutant to mutant, from mutant to malignant, from malignant cell to malignant cell, no death of normal cell, mutant cell, malignant cell is

$$1 - [\eta(a_{11} + b_{11} + c_{11}) + \mu(a_{21} + b_{21} + c_{21}) + \lambda(a_{31} + c_{31})]\Delta\tau + o(\Delta\tau)$$

Other events have a chance to happen with $o(\Delta\tau)^2$. The difference differential equation of the model is

$$\begin{aligned} P'_{\eta,\mu,\lambda}(\tau) = &-[\eta(a_{11} + b_{11} + c_{11}) + \mu(a_{21} + b_{21} + c_{21}) + \lambda(a_{31} + c_{31})]P_{\eta,\mu,\lambda}(\tau) \\ &+ (\eta - 1)a_{11}P_{\eta-1,\mu,\lambda}(\tau) + (\eta + 1)c_{11}P_{\eta+1,\mu,\lambda}(\tau) + (\mu - 1)a_{21}P_{\eta,\mu-1,\lambda}(\tau) \\ &+ (\mu + 1)c_{21}P_{\eta,\mu+1,\lambda}(\tau) + (\lambda - 1)a_{31}P_{\eta,\mu,\lambda-1}(\tau) + (\lambda + 1)c_{31}P_{\eta,\mu,\lambda+1}(\tau) \\ &+ (\eta + 1)b_{11}P_{\eta+1,\mu-1,\lambda}(\tau) + (\mu + 1)b_{21}P_{\eta,\mu+1,\lambda-1}(\tau) \text{ for } \eta, \mu, \lambda \geq 1. \quad (1) \end{aligned}$$

Let $p(l, m, n, \tau)$ be the joint probability generating function of $P_{\eta,\mu,\lambda}(\tau)$.

$$p(l, m, n, \tau) = \sum_{\lambda=0}^{\infty}\sum_{\mu=0}^{\infty}\sum_{\eta=0}^{\infty} l^{\eta}m^{\mu}n^{\lambda}p_{\eta,\mu,\lambda}(\tau) \quad (2)$$

Using the joint cumulant generating functions of $P_{\eta,\mu,\lambda}(\tau)$ to obtain its properties, Take $l = e^p$, $m = e^q$, $n = e^r$ and let $Q(p, q, r, \tau)$ be the joint cumulant generating functions of $P_{\eta,\mu,\lambda}(\tau)$. Let $w_{l,m,n}(\tau)$ denotes orderly moments and l, m, n denotes normal, mutant and malignant cells at time.

Equating the coefficients of p's, q's and r's. We get

$$\begin{aligned} \frac{\partial}{\partial\tau}w_{1,1,0}(\tau) = &-b_{11}w_{1,0,0}(\tau) + b_{11}w_{2,0,0}(\tau) + (a_{11} - c_{11} - b_{11})w_{1,1,0}(\tau) \\ &+ (a_{21} - c_{21} - b_{21})w_{1,1,0}(\tau) \quad (3) \end{aligned}$$

$$\frac{\partial}{\partial\tau}w_{1,0,1}(\tau) = (a_{11} - c_{11} - b_{11})w_{1,0,1}(\tau) + (a_{31} - c_{31})w_{1,0,1}(\tau) + a_{21}w_{1,1,0}(\tau) \tag{4}$$

$$\frac{\partial}{\partial\tau}w_{0,1,1}(\tau) = (b_{11} - a_{21})w_{0,1,0}(\tau) + b_{21}w_{0,2,0}(\tau) + (a_{21} - c_{21} - b_{21})w_{0,1,0}(\tau) + (a_{31} - c_{31})w_{0,1,1}(\tau) \tag{5}$$

$$\frac{\partial}{\partial\tau}w_{2,0,0}(\tau) = (a_{11} + c_{11} + b_{11})w_{1,0,0}(\tau) + 2(a_{11} - c_{11} - b_{11})w_{2,0,0}(\tau) \tag{6}$$

$$\frac{\partial}{\partial\tau}w_{0,2,0}(\tau) = b_{11}w_{1,0,0}(\tau) + 2b_{11}w_{1,1,0}(\tau) + 2(a_{21} - c_{21} - b_{21})w_{0,1,0}(\tau) + 2(a_{21} - c_{21} - b_{21})w_{0,2,0}(\tau) \tag{7}$$

Solving the above equations, we get

Relation between normal cells and Mutant cells at 'τ':

$$w_{1,1,0}(\tau) = \frac{b_{11}N_0De^{2A\tau}}{A(A-B)} + \frac{b_{11}N_0}{B}(1+D)e^{A\tau} - b_{11}N_0e^{(A+B)\tau}\left[\frac{D}{A} + \frac{1}{B}\left(1+\frac{D}{A}\right)\right] \tag{8}$$

Relation between Mutant cells and Malignant cells at 'τ':

$$w_{0,1,1}(\tau) = \frac{e^{2A\tau}}{2(A-B-C)}\left[\frac{b_{11}^2N_0D}{A(A-B)(A-C)} + \frac{2b_{21}b_{11}^2N_0D}{2A(A-B)^2}\right] + \frac{e^{A\tau}b_{11}N_0}{A-B-C}\left[b_{21}\left(1+\frac{2b_{11}}{B}+\frac{E}{A-B}\right) - \frac{b_{11}}{BC}\left(1+\frac{D}{A}\right) - \frac{1}{A-B}\right] - \frac{e^{B\tau}}{C}\left[b_{21}\left(\frac{b_{11}N_0E}{B(A-B)} - \frac{M_0}{B}\right) - M_0 + \frac{b_{11}N_0}{A-B}\right] + \frac{e^{2B\tau}b_{11}}{B-C}\left\{\begin{array}{l}\frac{b_{11}N_0D}{A(A-B)} + \frac{b_{11}N_0}{B}\left(1+\frac{D}{A}\right) - \frac{b_{11}N_0}{A-2B}\left(1+\frac{2b_{11}}{B}\right.\\ \left.+\frac{E}{A-B}\right) - \frac{b_{11}N_0E}{B(A-B)} - \frac{M_0}{B} - \frac{b_{11}^2N_0D}{A(A-B)^2}\end{array}\right\}$$

$$\frac{b_{11}^2 N_0 e^{(B-C)\tau}}{2C(B-C)}\left[\frac{D}{A}+\frac{1}{B}\left(1+\frac{D}{A}\right)\right]$$

$$-\frac{b_{11}^2 N_0 e^{(A+C)\tau}}{(A-B)}\left[\begin{array}{l}\frac{1}{BC}\left(1+\frac{D}{A}\right)+\frac{1}{B-C}\left[\frac{D}{A}+\frac{1}{B}\left(1+\frac{D}{A}\right)\right]\\ -\frac{D}{A(A-B)(A-C)}\end{array}\right]$$

$$-\frac{b_{21}b_{11}N_0 e^{(A+B)\tau}}{(A-B)}\left[\frac{D}{A}+\frac{1}{B}\left(1+\frac{D}{A}\right)\right]$$

$$-e^{(B+C)\tau}\left\{\frac{b_{11}^2 N_0 D}{A(A-B)(2A-B-C)}\left[\frac{1}{A-C}+\frac{b_{21}}{A-B}\right]\right.$$

$$+\frac{1}{A-B-C}\left[\begin{array}{l}\frac{b_{21}b_{11}N_0}{A-2B}\left(1+\frac{2b_{11}}{B}+\frac{E}{A-B}\right)\\ -\frac{b_{11}^2 N_0}{BC}\left(1+\frac{D}{A}\right)-\frac{b_{11}N_0}{A-B}\end{array}\right]$$

$$-\frac{b_{21}}{C}\left[\frac{b_{11}N_0 E}{B(A-B)}-\frac{M_0}{B}-M_0+\frac{b_{11}N_0}{A-B}\right]+\frac{b_{11}N_0}{B-C}$$

$$+\frac{b_{11}^2 N_0}{2C(B-C)}\left[\frac{D}{A}+\frac{1}{B}\left(1+\frac{D}{A}\right)\right]$$

$$-\frac{b_{11}N_0}{A-B}\left\{\begin{array}{l}\frac{b_{11}N_0}{BC}\left(1+\frac{D}{A}\right)\\ +\frac{b_{11}}{B-C}\left[\frac{D}{A}+\frac{1}{B}\left(1+\frac{D}{A}\right)\right]\\ -\frac{b_{11}N_0 D}{A(A-B)(A-C)}5\end{array}\right\}$$

$$\left.-\frac{b_{21}b_{11}N_0}{(A-B)}\left[\frac{D}{A}+\frac{1}{B}\left(1+\frac{D}{A}\right)\right]\right\},$$

where

$$A = a_{11} - b_{11} - c_{11},\ B = a_{21} - b_{21} - c_{21},\ C = a_{31} + c_{31}$$

$$D = a_{11} + b_{11} + c_{11},\ E = a_{21} + b_{21} + c_{21}$$

Illustration

The values accepted here are taken subjectively under specific uncertainties and it tends to be changed. The upshot of the moments depends correspondingly.

For the particular values of the parameters and varying the cells under virotheraphy, the analysis has been done and given below.

In the first figure, all the parameters values are fixed and the values of normal cells were varied, and the moment for the relation between the normal cells and the mutant cells have been plotted.

The second figure represents the relation between the mutant cells and malignant cells with the variation of values in the mutant cells.

The third figure represents the variation of the death of the malignant cells keeping all the other parameters fixed, the moment for the death of malignant cells is evaluated.

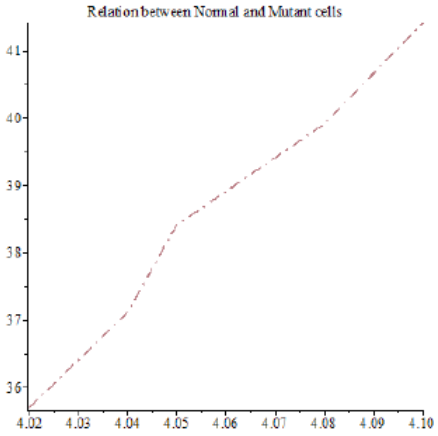


Figure 1.

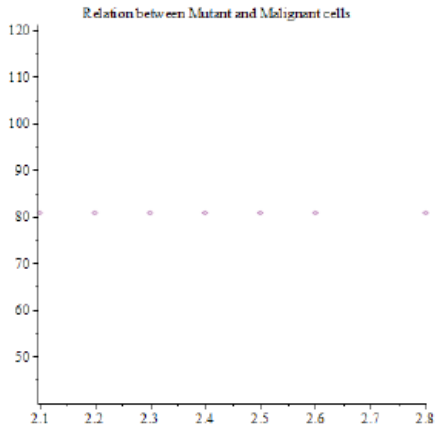


Figure 2.

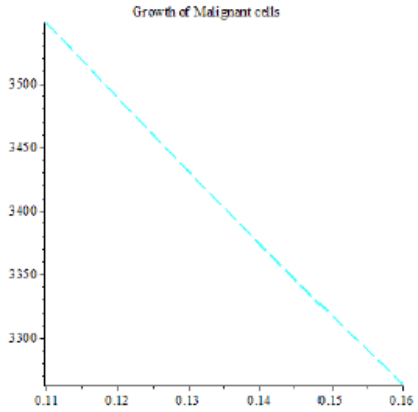


Figure 3.

Conclusion

It is found that the average growth of the malignant cells decreases with the continuous observation carried out under Oncolytic Virotheraphy. Also the relation between mutant and the malignant cells is observed to be stable under the treatment of Virotheraphy. Though this treatment has few complications to be resolved, it can be an emerging solution for the cancer treatment.

References

[1] D. G. Kendall, Birth and death processes and the theory of carcinogenesis, Biometrics 47 (1960), 13-121.

[2] B. G. Birkhead, The transient solution of the linear birth, Death Process with Random Spontaneous Mutation, Math. Bio. Sci. 82 (1986), 193-200.

[3] P. T. Rao and K. S. Rao, Stochastic model for cancer cell growth and spontaneous mutation and proliferation, International Journal of Management and Systems 20(1) (2004), 85-93.

[4] P. T. Rao and K. S. Rao, Two stage stochastic model for cancer cell growth, Indian Journal of Mathematics and Mathematical Sciences 2(2) (2006), 153-168.

[5] P. T. Rao, S. K. Masthan Babu and K. Madhavi, Bivariate stochastic modeling for mutant cell growth under chemotherapy, International Journal of Mathematics and Applications 4(1) (2011), 1-12.

[6] M. Abundo and C. Rossi, Numerical simulation of a stochastic model for cancerous cells submitted to chemotheraphy, Journal of Mathematical Biology, (1989), 81-90.

[7] John Carl Panetta, A mathematical model of drug resistance, Heterogeneous tumors Mathematical Biosciences 147(1) (1998), 41-61.