CANCER CELLGROWTH UNDER RADIOTHERAPY - USING TWO STAGE STOCHASTIC MODEL

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Abstract - ***In this paper, a two-phase stochastic model is created to contemplate malignancy cell development. In the first place, an ordinary clone becomes premalignant and later it gets malignant in the event that it takes further expansion. this circumstance inside the tumor development are typically befittingly approximated by building up a two-phase arbitrary model with the conviction that the extension of a premalignant cell, change, and loss of premalignant and malignant cells are irregular and follows Poisson procedure with totally various parameters. The joint likelihood producing a component of the quantity of premalignant and malignant cells inside tumor at a given time is determined by utilizing the distinction respectful conditions. The normal number of premalignant and malignant cells at a given time and their variances are additionally determined and investigated in the light of the parameters. The normal length of a malignant cell in the tumor and its fluctuation are determined and investigated.***

Keywords: ***two-stage stochastic model, Poisson process, premalignant cancer, malignant cancer, Optimum radiation scheduling.***

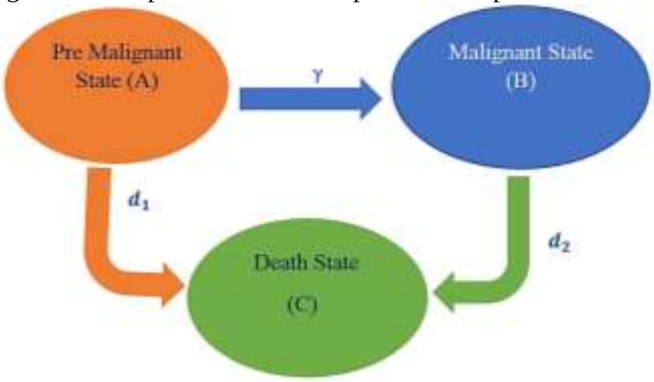
I. INTRODUCTION

A tumor is a mass of tissues framed in light of strange, unreasonable and unseemly expansion of cells. The crucial cycles of tumor development are unconstrained mutation, multiplication and misfortune cycle of the cell. The expansion of typical and freak cells are not homogeneous since the development and misfortune cycles of ordinary and freak cells are not same. Tumor development models portray the assessment and the size of tumor, which is thought to be begun from introductory changed cells. The quantity of cells in it approximates the size of tumor. The quantity of cells in tumor can for the most part be assessed in a roundabout way by estimating the volume, weight or substance markers of the tumor.

(a) A normal cell is divided into two normal cells,
(b) A normal cell is divided into a normal cell and a mutant cell,
(c) A mutant cell is divided into two mutant cells,
(d) A normal cell may be dead,
(e) A mutant cell may be dead in the small interval of time $(t, t + dt)$.

Let stage A denotes the normal cell is in pre malignant stage, Stage B denoted as malignant stage and Stage C denoted as the death of both malignant and pre malignant cells, which are in stage A and B. The diagram representing the transitions of the model is shown in figure 1.

Fig:1. Diagrammatic representation of the proliferation process of the tumor.



In this paper, two-stage stochastic model is developed with the assumption that the death of cell will occur in both states of pre malignant and malignant cells with open-ended models.

II. ASSUMPTIONS OF THE MODEL

1. The growth process of the malignant cells in the tumor is Poisson with parameters 'λ' in the state A. The transition of a malignant cell from state A to state B and from state A to state C are also Poisson with parameters 'γ' and 'd_1' respectively.
2. The transition from state B to state C is also Poisson with parameter d_2. The probability that a cell moves from state A to state B, when there are "n" cells in state 'A' during a small interval of time 'h' is $n\gamma h + o(h)$.
3. The probability that a cell moves from state A to state C, when there are "n" cells in state A during a small interval of time 'h' is $nd_1 h + o\,(h)$.
4. The probability that a cell moves from state B to state C, when there are "m" cells in the state B during a small interval of time "h" is $md_2 h + o(h)$.
5. The probability that there is a growth of pre malignant cell in state 'A' during the small interval of time 'h' is $\lambda h + o(h)$.
6. The probability that the occurrence of other than the above events during a small interval of time 'h' is $o(h)$ and.
7. The occurrences of events in non-overlapping intervals of time are stochastically independent.

III. MODEL DESCRIPTION

Let $P_{n,m}(t)$ be the probability that there are "n" cells in state A and "m" cells in state B during time 't' then the difference differential equations of the model are,

$$\frac{d}{dt}P_{n,m}(t) = -(md_2 + nd_1 + n\gamma + \lambda)P_{n,m}(t) + \lambda P_{n-1,m}(t) + (n+1)\gamma P_{n+1,m-1}(t) + (n+1)\ d_1 P_{n+1,m}(t) + (m+1)d_2 p_{n,m+1}(t), for\ n,m \geq 1 \quad ...(1)$$

$$\frac{d}{dt}P_{0,0}(t) = -\lambda P_{0,0}(t) + d_1 P_{1,0}(t) + d_2 P_{0,1}(t) \quad ...(2)$$

$$\frac{d}{dt}P_{1,0}(t) = -(\lambda + d_1 + \gamma)p_{1,0}(t) + 2d_1 P_{2,0}(t) + d_2 P_{1,1}(t) + \lambda P_{0,0}(t) \quad ...(3)$$

$$\frac{d}{dt}P_{0,1}(t) = -(\lambda + d_2)p_{0,1}(t) + d_1 P_{1,1}(t) + \gamma 1 P_{1,0}(t) + d_2 P_{0,2}(t) \quad ...(4)$$

Let $P(x,y,z)$ denote the joint probability generating function of $P_{n,m}(t)$,

$$P(x,y;t) = \sum_{n=0}\sum_{m=0} x^n y^m P_{n,m}(t); \qquad |x| < 1, |y| < 1 \quad ...(5)$$

Multiplying the equation (1) to (4) with $x^n\ and\ y^m$ and summing over all 'n' and 'm' and adding we get

$$\frac{d}{dt}P(x,y:t) = -\lambda\left[\sum_n\sum_m x^n y^m P_{n,m}(t) - \sum_n\sum_m xx^{n-1}y^m P_{n-1,m}(t)\right] + d_1\left[\sum_n\sum_m (n+1)x^n y^m P_{n+1,m}(t) - \sum_n\sum_m nxx^{n-1}y^m P_{n,m}(t)\right] - \beta\left[\sum_n\sum_m nxx^{n-1}y^m P_{n,m}(t) - \sum_n\sum_m (n+1)x^n yy^{m-1}P_{n+1,m-1}(t)\right] - d_2\left[\sum_n\sum_m mx^n yy^{m-1}P_{n,m}(t) - \sum_n\sum_m (m+1)x^n y^m P_{n,m+1}(t)\right] \quad \ldots(6)$$

After simplification, we get

$$\frac{d}{dt}P(x,y:t) = [-(d_1+\gamma)x - \gamma y + d_1]\frac{\partial P}{\partial x} + d_2(1-y)\frac{\partial P}{\partial y} - \lambda P(1-x)$$

Which can be rearranged as

$$\frac{dP}{dt} - [-(d_1+\gamma)x - \gamma y + d_1]\frac{\partial P}{\partial x} - d_2(1+y)\frac{\partial P}{\partial y} = P\lambda(x-1) \quad \ldots(7)$$

Solving the equation (7) using the Lagrange's method,

We have

$$\underset{(i)}{\frac{dt}{1}} = \underset{(ii)}{\frac{-dx}{-(d_1+\gamma)x-\gamma y+d_1}} = \underset{(iii)}{\frac{-dy}{d_2(1-y)}} = \underset{(iv)}{\frac{dp}{\lambda(x-1)p}} \quad \ldots(8)$$

Solving the system of equation $(i), (ii), (iii)$ and (iv) in (8), pair wise we get the arbitrary constants a, b, c as

$$a = e^{-d_2 t}(y-1) \quad \ldots.(9)$$

$$b = \left[(1-x) - \frac{\gamma}{d_1+\gamma-d_2}(1-y)\right](1-y)^{-\left(\frac{d_1+\gamma}{d_2}\right)} \quad \ldots.(10)$$

$$c = P\,exp\left\{\frac{\lambda}{d_1+\gamma}(1-x) + \frac{\gamma}{d_1+\gamma}(1-y)\right\} \quad \ldots(11)$$

Using the arbitrary constants given in equation (9), (10) & (11) the general solution of (7) can be obtained as

$$P(x,y,t) = exp\left\{\frac{\lambda}{d_1+\gamma}(1-x) + \frac{\gamma}{d_1+\gamma}(1-y)\right\} \Psi\left[e^{-d_2 t}(1-y)\left\{(1-x) - \frac{\beta}{d_1+\beta-d_2}(1-y)\right\}(1-y)^{-\left(\frac{d_1+\beta}{d_2}\right)}\right] \quad \ldots(12)$$

Where Ψ, is an arbitrary function of two variables.

Therefore substituting the initial condition $P_{N_0,M_0}(0) = 1$, we get

$$P(x,y,t) = exp\left\{\frac{\lambda}{d_2}\left\{\frac{-d_2}{d_1+\gamma}(1-x)\left(1-e^{-(d_1+\gamma)t}\right) - \left[\frac{\gamma}{d_1+\gamma}(1-y)(1-e^{-d_2 t})\right] - \left[\frac{d_2\gamma(1-y)(e^{-d_2 t}-e^{-(d_1+\gamma)t})}{(d_1+\gamma)(d_1+\gamma+d_2)}\right]\right\}\right\}\left[1-(1-x)e^{-(d_1+\gamma)t} - \frac{\gamma}{d_1+\gamma-d_2}(1-y)\left((e^{-d_2 t} - e^{-(d_1+\gamma)t}\right)\right]^{N_0}\left[1-(1-y)e^{-d_2 t}\right]^{M_0} \quad \ldots(13)$$

The Average number of cells in state A at time 't' is

$$E[N(t)] = \frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right) + N_0 e^{-(d_1+\gamma)t} \quad \ldots(14)$$

The Average number of cells in state B at time 't' is

$$E[M(t)] = \left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2} - \frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right] + \left(\frac{N_0\gamma}{d_1+\gamma-d_2}\right)\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)M_0 e^{-d_2t} \quad \ldots(15)$$

The variance of the number of cells in state A is

$$V[N(t)] = \left[\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right)\right]^2 + N_0(N_0-1)e^{-2(d_1+\gamma)t} + \left(\frac{2\lambda N_0}{d_1+\gamma}\right)\left(1-e^{-(d_1+\gamma)t}\right)\left(e^{-(d_1+\gamma)t}\right) + \left[\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right) + N_0 e^{-(d_1+\gamma)t}\right]\left[1 - \left\{\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right) + N_0 e^{-(d_1+\gamma)t}\right\}\right] \quad \ldots(16)$$

The variance of the number of malignant cells in state B is obtained as

$$V[M(t)] = \left\{\left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2} - \frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right]^2 + N_0(N_0-1)\left[\left(\frac{\gamma}{d_1+\gamma-d_2}\right)\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)\right]^2 + e^{-d_2t}(M_0-1)e^{-2d_2t} + 2N_0M_0\gamma e^{-d_2t}\left[\frac{\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2}\right] + 2\left[\frac{\gamma N_0\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2} + M_0e^{-d_2t}\right]\left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2} - \frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right]\right\} + \left\{\left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2} - \frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right] + \left[\frac{\gamma N_0\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2} + M_0e^{-d_2t}\right]\right\}\left\{1 - \left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2} - \frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right] + \left[\frac{\gamma N_0\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2} + M_0e^{-d_2t}\right]\right\} \quad \ldots(17)$$

The covariance between the number of cells in state A and in State B is

$$Cov\,[M(t),N(t)] = \left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2} - \frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right]\left[\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right) + N_0e^{-(d_1+\gamma)t}\right] + \left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)\frac{\gamma N_0}{d_1+\gamma-d_2}\left[(N_0-1)e^{-(d_1+\gamma)t} + \frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right)\right] + \left[\frac{\lambda M_0}{d_1+\gamma}e^{-d_2t}\left(1-e^{-(d_1+\gamma)t}\right) + N_0M_0e^{-(d_1+\gamma+d_2)t}\right] - \left\{\left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2} - \frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right] + \left[\frac{\gamma N_0\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2} + M_0e^{-d_2t}\right]\right\}\left[\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right) + N_0 - e^{-(d_1+\gamma)t}\right] \quad \ldots(18)$$

The average total number of pre malignant and malignant cells in the tumor in both states A and B is

$$E[L(t)] = E[N(t)] + E[M(t)]$$

$$E[L(t)] = \left[\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right) + N_0e^{-(d_1+\gamma)t}\right] + \left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2} - \frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right] + \left(\frac{N_0\gamma}{d_1+\gamma-d_2}\right)\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)M_0e^{-d_2t} \quad \ldots.(19)$$

The variability of total number of cells in both the states is obtained from

$$V[L(t)] = \left[\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right)\right]^2 + N_0(N_0-1)e^{-2(d_1+\gamma)t} + \left(\frac{2\lambda N_0}{d_1+\gamma}\right)\left(1-e^{-(d_1+\gamma)t}\right)\left(e^{-(d_1+\gamma)t}\right)$$
$$+\left[\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right)+N_0e^{-(d_1+\gamma)t}\right]\left[1-\left\{\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right)+N_0e^{-(d_1+\gamma)t}\right\}\right]$$
$$+\left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2}-\frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right]^2$$
$$+N_0(N_0-1)\left[\left(\frac{\gamma}{d_1+\gamma-d_2}\right)\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)\right]^2$$
$$+M_0(M_0-1)e^{-2d_2t}\ 2\left[\frac{\gamma N_0\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2}\right.$$
$$\left.+M_0e^{-d_2t}\right]\left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2}-\frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right]+2N_0M_0\gamma e^{-d_2t}\left[\frac{\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2}\right]$$
$$+\left\{\left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2}-\frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right]+\left[\frac{\gamma N_0\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2}+M_0e^{-d_2t}\right]\right\}\left\{1\right.$$
$$\left.-\left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2}-\frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right]+\left[\frac{\gamma N_0\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2}+M_0e^{-d_2t}\right]\right\}$$
$$-\left\{2\left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2}-\frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right]\left[\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right)+N_0e^{-(d_1+\gamma)t}\right]\right.$$
$$+\left[\frac{\gamma N_0\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2}\right]\left[\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right)+(N_0-1)e^{-(d_1+\gamma)t}\right]$$
$$\left.+\left[\frac{\lambda\gamma}{d_1+\gamma}e^{-d_2t}\left(1-e^{-(d_1+\gamma)t}\right)+N_0M_0e^{-(d_1+\gamma+d_2)t}\right]\right\}$$
$$+2\left\{\left[\frac{\lambda}{d_1+\gamma}\left(1-e^{-(d_1+\gamma)t}\right)+N_0e^{-(d_1+\gamma)t}\right]\left[\frac{\lambda\gamma}{d_1+\gamma}\left\{\frac{1-e^{-d_2t}}{d_2}-\frac{e^{-d_2t}-e^{-(d_1+\gamma)t}}{d_1+\gamma-d_2}\right\}\right]\right.$$
$$\left.+\left[\frac{\gamma N_0\left(e^{-d_2t}-e^{-(d_1+\gamma)t}\right)}{d_1+\gamma-d_2}+M_0e^{-d_2t}\right]\right\} \qquad \ldots(20)$$

For various values of $t,\ \lambda, d_1, \gamma, M_0, N_0, d_2, E[L(t)], V[L(t)]$ are given in table 1.

TABLE-1

Values of $E[L(t)]$, $V[L(t)]$ for various values of the parameters

λ	d_1	γ	d_2	M_0	N_0	t	$E[L(t)]$	$V[L(t)]$
0.934	0.021	0.784	0.237	10	15	5	12.629	35.565
			0.351				8.985	33.92
			0.465				6.701	32.45
			0.543				5.636	31.653
1.432	0.0875	0.082	0.0762	10	15	5	22.434	176.468
		0.234					22.590	130.150
		0.386					22.691	112.014
		0.538					22.759	107.623
1.432	0.124	0.029	0.462	2	5	5	7.909	106.404
	0.276						5.232	82.234
	0.325						4.653	78.426
	0.395						3.987	75.205
0.491	0.015	0.009	0.462	20	5	5	8.842	77.285
0.684							9.762	112.819
0.951							11.036	167.64
1.430							13.320	282.866
0.684	0.015	0.009	0.462	10	5	5	17.801	111.925
						8	17.926	187.419
						10	18.313	241.799
						12	18.763	299.224

0.951	0.015	0.009	0.462	20	10	5	15.551	124.928
				40			17.536	126.717
				60			19.521	128.505
				80			21.507	130.293
0.987	0.775	0.009	0.862	40	20	5	2.195	42.186
						7	1.449	103.852
						9	1.306	402.962
						10	1.287	852.918
0.987	0.775	0.009	0.862	2	4	5	1.355	21.225
					6		1.396	23.782
					8		1.437	26.340
					9		1.458	27.618
0.987	0.775	0.009	0.862	5	4	5	1.395	21.265
				6			1.409	21.278
				7			1.422	21.292
				8			1.436	21.305

MODEL FOR CELL DURATION IN THE CANCER

In this model, we assume that every malignant cell in the tumor is in state (A) in the beginning. After a period of time in state A, the malignant cell will either dead (going to state C) or divides in to two mutant cells (going to state B).

Let f(x) be the probability density function of a cell that the time spent in state A until leaving to state 'C'. Let $g(x)$ be the probability density function of the time that a cell will spent in state 'A' until leaving to state B and h(x) be the probability density function of a cell that the time spent in state B until leaving to state 'C'.

Then the survival function of the cell in the states A, B and C respectively are

$$F(t) = 1 - \int_0^t f(x)\,dx \qquad \text{... (21)}$$

$$G(t) = 1 - \int_0^t g(x)\,dx \qquad \text{... (22)}$$

$$H(t) = 1 - \int_0^t h(x)\,dx \qquad \text{... (23)}$$

Therefore the force of transition from state A to state C, state A to state B and state B to state C respectively are

$$\Psi_1(t) = \frac{f(t)}{F(t)} \qquad \text{... (24)}$$

$$\Psi_2(t) = \frac{g(t)}{G(t)} \qquad \text{... (25)}$$

$$\Psi_3(t) = \frac{h(t)}{H(t)} \qquad \text{... (26)}$$

The probability that a malignant cell generated initially at time t=0 is still in the tumor in state A at time't' is

$$a(t) = \int_t^\infty [F(x)g(x) + G(x)f(x)]dx \qquad \text{... (27)}$$

The probability that a mutant malignant cell in state 'B' at time't' is

$$b(t) = \int_0^t \left[\int_t^\infty [F(y)g(y) + G(y)f(y)]dy\right] \frac{g(x)H(t-x)}{G(x)} dx \qquad \text{... (28)}$$

The probability that a malignant (either mutant or pre mutant) cell is in state 'C' at time 't' is ,

$$c(t) = 1 - a(t) - b(t) \qquad \text{for all } t \geq 0 \qquad \text{... (29)}$$

In order to analyze transition probabilities, we assume that the duration of time a cell spent in state A before reaching to state B; the duration of time a cell in the state B before reaching to state C and the duration of time a cell in the state 'A' before reaching to state C are all exponential with parameters γ, d_1 and d_2 respectively.

$$\left.\begin{aligned} f(x) &= d_1 e^{-d_1 x} \\ g(x) &= \gamma e^{-\beta x} \\ h(x) &= d_2 e^{-d_2 x} \end{aligned}\right\} \qquad \text{... (30)}$$

Therefore the expected duration of a pre malignant cell is in state A before reaching state C is $(1/d_1)$ the expected duration of pre malignant cell in state A before reaching the state B is $(1/\gamma)$ and the expected duration of a mutant malignant cell in state B before reaching state C is $(1/d_2)$.

Substituting (31) in the equations (28), (29) and in (30) we get

$$a(t) = e^{-(d_1+\gamma)t} \quad \text{... (31)}$$

$$b(t) = \frac{\gamma}{d_1+\gamma-d_1}\left(e^{-d_2 t} - e^{-(d_1+\gamma)t}\right) \quad \text{... (32)}$$

$$c(t) = 1 - \left(\frac{d_1-d_2}{d_1+\gamma-d_2}\right)e^{-(d_1+\gamma)t} - \left(\frac{\beta}{d_1+\gamma-d_1}\right)e^{-d_2 t} \quad \text{... (33)}$$

Let $s(t)$ be the probability that a pre-malignant cell generated at time $t = 0$ is still in the tumor at time 't', then

$$s(t) = Pe^{-\lambda_1(t)} + (1-P)e^{-\lambda_2(t)} \quad \text{... (34)}$$

Where,

$$\lambda_1 = d_1 + \gamma$$
$$\lambda_2 = d_2$$
$$P = \frac{d_1 - d_2}{d_1 + \gamma - d_2}$$

Therefore $s(t)$ is the Probability density function of the mixture of exponential distribution with parameters P, λ_1, λ_2.

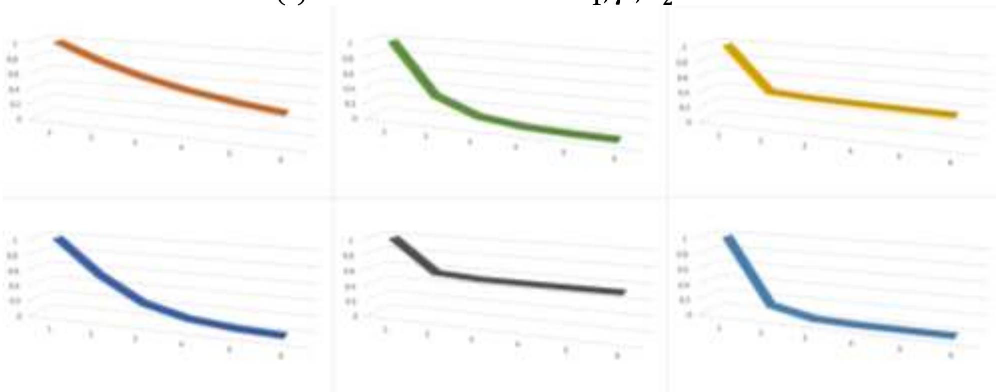
For different values of d_1, γ, d_2 and t the values of $s(t)$ are computed and given in table 2.

Table -2

The values of $S(t)$ for different values of d_1, γ, d_2 and t

Cyclic	d_1	γ	d_2	t	S(t)
	0.1234	0.0174	0.0013	0	1
				2	0.785
				4	0.622
I				6	0.500
				8	0.407
				10	0.337
	0.5674	0.0174	0.4562	0	1
				2	0.323
				4	0.105
II				6	0.035
				8	0.012
				10	0.004
	0.9845	0.6834	0.174	0	1
				2	0.421
				4	0.387
III				6	0.373
				8	0.360
				10	0.348
	0.1234	0.9845	0.4532	0	1
				2	0.553
				4	0.239
IV				6	0.098
				8	0.040
				10	0.016
	0.5674	0.6834	0.0013	0	1
				2	0.582
				4	0.547
V				6	0.543
				8	0.541
				10	0.540
	0.9845	0.9903	0.9744	0	1
				2	0.141
				4	0.020
VI				6	0.003
				8	0.00041
				10	0.000058

$S(t)$ for different values of d_1, γ , d_2 and t



IV. CONCLUSION

Table - 1

- From the equation (19) and Table-1, we observe that the average total number of cells in the tumor at a given time 't' is an decreasing function of d_2 when $(\lambda+\gamma) > (d_1 + d_2)$.
- It is also observed that $E[L(t)]$ is an increasing function of γ as $(\lambda+\gamma) > (d_1 + d_2)$ and $M_0 < N_0$. The mean number of cells in the tumor at a given time 't' is an decreasing function of d_1 as $(\lambda+\gamma) > (d_1 + d_2)$.
- It is further observed that $E[L(t)]$ is an increasing function of 'λ' as $(\lambda+\gamma) > (d_1 + d_2)$ when other parameters remain fixed. $E[L(t)]$ is an increasing function of 't' as $(\lambda+\gamma) > (d_1 + d_2)$.
- From the equation (20) and Table -1 It is observed that the variability of total number of cells in the tumor is an increasing function of λ.
- It is further observed that $V[L(t)]$ is an increasing function of both M_0 and N_0.

Table - 2

- From table -2 we observe that $s(t)$ is a decreasing function of 't' when other parameters remain fixed. Let 't' be the total duration of a cells in the tumor before reaching state C.

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