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# Novel Technique to Investigate the Effect of Different Drugs of Chemotherapy to GlioblastomaTumor Cells Growth and Invasion in Homogeneous Medium

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**ABSTRACT**

Cancerous tumors from the mutations of one or more cells which usually undergo rapid uncontrolled growth thereby are impairing the functioning of normal tissues. There are many different types of cancers, we concerned with the brain tumor predominantly Glioblastoma, which make up about half of all primary brain tumors diagnosed. It is very nasty tumors with a depressingly dismal prognosis for recovery. We believe that model could be used to make predictions regarding the survival time of the patient following the various types of treatments including resection, radiation and chemotherapy. For clarification of the models we established the Kamal Variational Iteration Method (KVIM).

KVIM gives rapidly convergent successive approximations without any restrictive assumptions or transformations which may change the physical behaviour of the problem. Kamal Transform is a new arrival of an integral transform which is useful to apply to find the Lagrange Multiplier in VIM method. Generally it is difficult to crack out. Using the Kamal Transform it's become easier to find the same and one can hoard the time.

Aim of this research is to thrash out the current developments of the methods to crack the mathematical models of effect of different drugs used in chemotherapy treatment upon Glioblastomatumor cells growth and invasion when early cancer cells are known and unknown when both appeared in Homogeneous medium. It might be unlock the doors for improvement in prediction of recovery of the patient.

**Keywords:**
GlioblastomaTumor, White and Gray Matter, Homogeneous Medium, Chemotherapy, Kamal Variational Iteration Method.

## Introduction

Glioblastoma also known as Glioblastoma multiform (GBM), is a fast growing tumor develops from glial cells that supports the health of the nerve cells within the brain. GBM is high grade IV, most invasive type of glial tumors, rapidly growing and commonly spreading into nearby brain tissues. It mainly occurs in adults and rarely occurs in children. GBM is a devastating brain cancer that typically results in death in the first 15 months after diagnosis [W1].

Brain tumors, whether primary or metastatic, benign or malignant, usually are treated with surgery, radiation, and/or chemotherapy- alone or in various combinations. While it is true that radiation and chemotherapy are used more often for malignant, residual or recurrent tumors, decisions as to what treatment to use are made on a case-by-case basis and depends on a number of factors. There are risks and side effects associated with each type of therapy [W2]. So sometimes doctors are not prefer chemotherapy for some patients.

To solve the mathematical model of applying the different drugs of chemotherapy upon GlioblastomaTumor cells growth and invasion in homogeneous medium when early cancer cells

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are known and unknown, we will use the combination of the new arrival of transform – Kamal Transform and Variational Iteration Method- Kamal Variational Iteration Method.

## Methodology:

Kamal transform was introduced by Abdelilah Kamal in 2016 [17], for soft growth of the process of solving ordinary and partial differential equations from time domain to frequency domain.

Kamal Transform is denoted and defined as, [17]

$$K\left[ f\left(t\right)\right] = T\left(u\right) = \int_0^\infty e^{-\frac{t}{u}} f\left(t\right) dt \; ; t \geq 0, m_1 < u < m_2$$

.

**Kamal Variational Iteration Method (New KVIM): [17, 20]**

To exemplify the design of Kamal Variational Iteration Method, we consider the general differential equation, as

$$L\left[\mathrm{C}\left(x,t\right)\right] + N\left[\mathrm{C}\left(x,t\right)\right] = h(x,t) \tag{1}$$

Where $L$ is a Linear partial differential operator given by $\frac{\partial^2}{\partial t^2}$, $N$ is a nonlinear operator and $h(x,t)$ is an analytical continuous source function.

According to the Variational Iteration Method, we can construct a correctional function for (1),

$$\mathrm{C}_{n+1}\left(x,t\right) = \mathrm{C}_n\left(x,t\right) + \int_0^t \lambda(x,\tau)\left[ L\left[\mathrm{C}_n\left(x,\tau\right)\right] + N[\tilde{\mathrm{C}}_n\left(x,\tau\right)] - h(x,\tau)\right] d\tau, n \geq 0$$

(2)

Where $\lambda$ is a general Lagrange Multiplier, which can be identified optimally via variationaltheory. $\tilde{\mathrm{C}}_n$ is restricted variation. i.e. $\delta\tilde{\mathrm{C}}_n = 0$.

Take Kamal Transform on both the sides of (2), and doing integration by parts, we get the iteration formula for KVIM as;

$$\therefore K\left[\mathrm{C}_{n+1}\left(x,t\right)\right] = K\left[\mathrm{C}_n\left(x,t\right)\right] + K\left[-t\right]\cdot K\left[ L\left[\mathrm{C}_n\left(x,t\right)\right] + N\left[\mathrm{C}_n\left(x,t\right)\right] - h\left(x,t\right)\right] \tag{3}$$

**Mathematical Models of Effect of different drugs in Chemotherapy to GlioblastomaTumor Cells Growth and Invasion in Homogeneous Medium: [10]**

We have taken in account the model developed by Cruywagen et al. and Tracqui et al.[3,4] to quantify the effect of different drugs to chemotherapy on tumor growth. This model estimated with parameters to give the best fit of the simulated tumor area to the CT scan data. We carried out numerical simulations on one dimensional domain. Drugs, Combination of drugs in chemotherapy are decided regarding to many factors and also depends upon the patient's cell structure, where it has been placed, how much it spread out etc. In our data the value $K_1$ is taken for a course of six drugs- 6-thioguanine,procarbazine, dibromodulcitol, CCNN, 5-florouracil and hydroxyurea given over 15 days and repeated every six to eight weeks to allow for recovery of bone marrow [10], and the value $K_2$ is taken for Cisplatinum drug.

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To quantify the effect of drugs of chemotherapy model taken in account is,

$$\frac{\partial C}{\partial t} = D\nabla^2 C + \rho C - K(t)C \quad (4)$$

Where $C$: Cell Density or No. of cells, $t$ : Time , $\rho$: Growth Rate, $D$: Diffusion Coefficient, $K(t)C$ : No. of cells killed through drugs.

As we are examine the Effect of different drugs of Chemotherapy to GlioblastomaTumor cells growth and Invasion in homogeneous medium that means tumors are detected in White matter or in Gray Matter only.

**Case:1 When spread of early cancer cells are unknown:**

$$\frac{\partial W}{\partial t} = D\frac{\partial^2 W}{\partial x^2} + \rho W - K_i W \quad ; W(x,0) = W_0$$ (White Matter) [9,10] or (5)

$$\frac{\partial G}{\partial t} = D\frac{\partial^2 G}{\partial x^2} + \rho G - K_i G \quad ; G(x,0) = G_0$$ (Gray Matter) [9,10] (6)

Applying KVIM method, we get the solution; $W(x,t) = W_0 e^{(\rho - K_i)t}$ & $G(x,t) = G_0 e^{(\rho - K_i)t}$

**Numerical Parameters:**

| **Parameters** | **White Matters** | **Gray Matters** |
|---|---|---|
| No. of Cells | $W_0 = 20,000\ cells/cm^2$ | $G_0 = 8000\ cells/cm^2$ |
| High $\rho$ | $\rho_W = 0.012\ cm/day$ [9,10] | $\rho_G = 0.012\ cm/day$ [9,10] |
| Low $\rho$ | $\rho_W = 0.008\ cm/day$ [9,10] | $\rho_G = 0.008\ cm/day$ [9,10] |
| $K_1$-Combination of Six Drugs | 0.0391 [9,10] | 0.0391 [9,10] |
| $K_2$-Cisplatinum | 0.0285 [9,10] | 0.0285 [9,10] |

**Graphical Representation:**

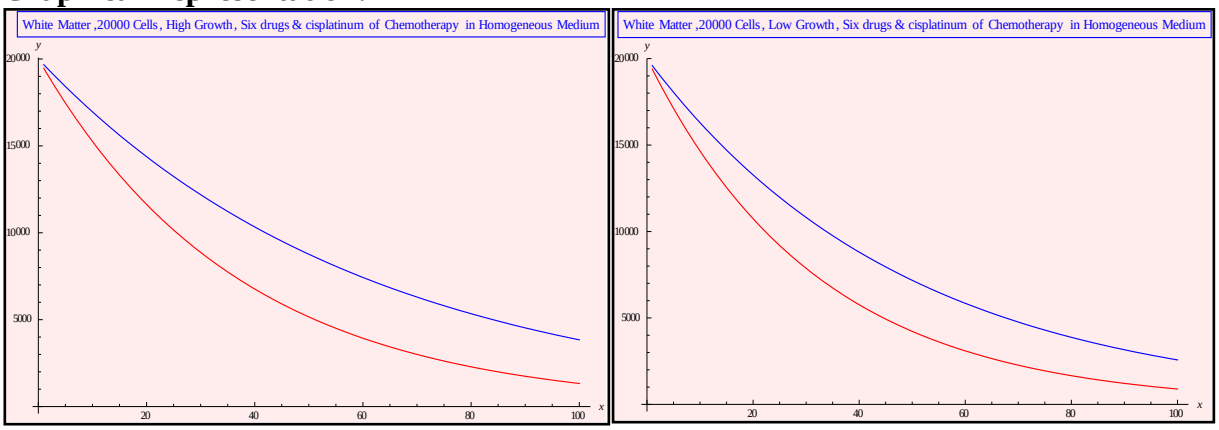


**Fig.1 White Matter, High Growth, Six Drugs &Cisplatinum, 20000 Cells**
**Fig.2 White Matter, Low Growth, Six Drugs &Cisplatinum, 20000 Cells**

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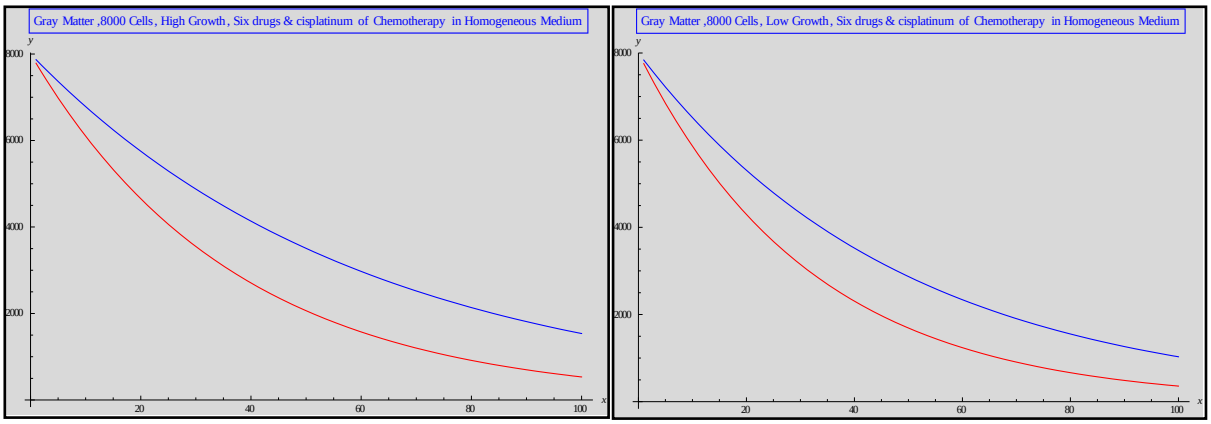


**Fig.3 Gray Matter, High Growth, Six Drugs &Cisplatinum, 8000 Cells**
**Fig.4 Gray Matter, Low Growth, Six Drugs &Cisplatinum, 8000 Cells**
(Combination of Six Drugs-Red Line &Cisplatinum- Blue Line)

**Conclusion of case-1:**
We can conclude from the graph that, in white matter for high growth rate, no. of cells are decreasing from 20,000 to 100 cells using six drugs combination, while using Cisplatinum no. of cells are reducing to 4000 cells. While in Gray Matter for high growth rate, no. of cells are decreasing from 8,000 to 500 cells using six drugs combination, while using Cisplatinum no. of cells are reducing to 1800 cells.

**Case:2 When spread of early cancer cells are known:**

$$\frac{\partial W}{\partial t} = D\frac{\partial^2 W}{\partial x^2} + \rho W - K_i W \quad ; W(x,0) = W_0\, e^{-\frac{|x-x_0|^2}{b}} \qquad [9,10] \qquad (7)$$

$$\frac{\partial G}{\partial t} = D\frac{\partial^2 G}{\partial x^2} + \rho G - K_i G \quad ; \quad G(x,0) = G_0\, e^{-\frac{|x-x_0|^2}{d}} \qquad [9,10] \qquad (8)$$

Using KVIM, we get the iteration formulas in White and Gray Matter as,

$$W_1(x,t) = W_0\, e^{-\frac{|x-x_0|^2}{b}}\left[1 - \frac{2Dt}{b} + \frac{4Dt|x-x_0|^2}{b^2} + \rho t - K_i t\right]$$

$$G_1(x,t) = G_0\, e^{-\frac{|x-x_0|^2}{d}}\left[1 - \frac{2Dt}{d} + \frac{4Dt|x-x_0|^2}{d^2} + \rho t - K_i t\right]$$

$$W_2(x,t) = W_0\, e^{-\frac{|x-x_0|^2}{b}}\left[1 - \frac{2Dt}{b} + \rho t - K_i t + \frac{4Dt|x-x_0|^2}{b^2} + \frac{6D^2t^2}{b^2} - \frac{2D\rho t^2}{b} + \frac{2K_i Dt^2}{b} + \frac{4\rho Dt^2|x-x_0|^2}{b^2} - \frac{4K_i Dt^2|x-x_0|^2}{b^2} + \frac{\rho^2 t^2}{2} + \frac{K_i^2 t^2}{2} - \rho K_i t^2 - \frac{24D^2t^2|x-x_0|^2}{b^3} + \frac{8D^2t^2|x-x_0|^4}{b^4}\right]$$

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$$G_2(x,t) = G_0 e^{-\frac{|x-x_0|^2}{d}} \left[ \begin{array}{l} 1 - \frac{2Dt}{d} + \rho t - K_i t + \frac{4Dt|x-x_0|^2}{d^2} + \frac{6D^2t^2}{d^2} - \frac{2D\rho t^2}{d} + \frac{2K_iDt^2}{d} + \frac{4\rho Dt^2|x-x_0|^2}{d^2} \\ - \frac{4K_iDt^2|x-x_0|^2}{d^2} + \frac{\rho^2 t^2}{2} + \frac{K_i^2 t^2}{2} - \rho K_i t^2 - \frac{24D^2t^2|x-x_0|^2}{d^3} + \frac{8D^2t^2|x-x_0|^4}{d^4} \end{array} \right]$$

And so on..

For calculation we considered second iteration. No. of cells are taken highest as 40000 and lowest as 500. Tumors with more than 40000 cells, it's difficult to survive for patients, while Tumors less than 500 cells are generally not detected in CT scan.

**Numerical Parameters: For HH Grade (High $\rho$, High $D$)**

| Parameters | White Matter | Gray Matter |
|---|---|---|
| Velocity of Cells | $v_W = 0.018\ cm/day$ [9,10] | $v_G = 0.008\ cm/day$ [9,10] |
| Diffusion Rate | $D_W = 0.0065\ cm^2/day$ [9,10] | $D_G = 0.0013\ cm^2/day$ [9,10] |
| Growth Rate | $\rho_W = 0.012\ cm/day$ [5,6] | $\rho_G = 0.012\ cm/day$ [9,10] |
| Number of Cells | $W_0 = a = 40000$ & 500 | $G_0 = c = 40000$ & 500 |
| Measure of spread of tumor cells | $b = 0.8$ cm | $d = 0.4$ cm |
| Centre | $x_0 = 0$ | $x_0 = 0$ |
| $K_1$-Combination of Six Drugs | 0.0391 [9,10] | 0.0391 [9,10] |
| $K_2$-Cisplatinum | 0.0285 [9,10] | 0.0285 [9,10] |

**Table: 1 Case-2 HH Grade, White Matter, 40000 cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39503.1 | 38049.2 | 35743.9 | 32749.2 | 29264.6 | 25505.1 | 21679.8 | 17973.2 | 14532.4 | 11460.2 |
| **10** | 27256.8 | 26443.8 | 24984.8 | 23154. | 20959. | 18925.2 | 16433.3 | 14036.8 | 11901.6 | 9843.9 |
| **20** | 24490.5 | 23208.4 | 20873.7 | 18340.8 | 15415.4 | 13519.3 | 10709.8 | 8374.36 | 6944.78 | 5705.6 |
| **30** | 31204.2 | 28343. | 23410.6 | 18309.6 | 12633.8 | 9287.43 | 4509.27 | 985.96 | -338.02 | -954.7 |
| **40** | 47397.9 | 41847.6 | 32595.5 | 23060.4 | 12614.2 | 6229.53 | -2168.23 | -8128.44 | -9946.82 | -10137. |
| **50** | 73071.6 | 63722.2 | 48428.4 | 32593.2 | 15356.6 | 4345.63 | -9322.73 | -18968.8 | -21881.6 | -21841.3 |
| **60** | 108225. | 93966.8 | 70909.3 | 46908. | 20861. | 3635.73 | -16954.2 | -31535.2 | -36142.4 | -36067.6 |
| **70** | 152859. | 132581. | 100038. | 66004.8 | 29127.4 | 4099.83 | -25062. | -45827. | -52729. | -52815. |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 7 | 6 | 2 | 9 |
| **80** | 206973. | 179566. | 135815. | 89883.6 | 40155.8 | 5737.93 | -33648.2 | -61846. | -71642. | -72086.2 |
| **90** | 270566. | 234921. | 178240. | 118544. | 53946.2 | 8550.03 | -42710.7 | -79590.4 | -92880.8 | -93878.5 |
| **100** | 343640. | 298645. | 227313. | 151987. | 70498.6 | 12536.1 | -52250.2 | -99060.8 | -116446. | -118193. |

**Table: 1a Case-2 HH Grade, White Matter, 40000 cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| **t** | **x=0.1** | **x=0.2** | **x=0.3** | **x=0.4** | **x=0.5** | **x=0.6** | **x=0.7** | **x=0.8** | **x=0.9** | **x=1** |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39503.1 | 38049.2 | 35743.9 | 32749.2 | 29264.6 | 25505.1 | 21679.8 | 17973.2 | 14532.4 | 11460.2 |
| **10** | 29904.1 | 28917. | 27415.2 | 25511.4 | 23213.1 | 18491.2 | 18319.8 | 15744.9 | 13442.1 | 11173.3 |
| **20** | 26389.1 | 25110.8 | 23160.5 | 20827.6 | 18227.6 | 6631.33 | 13659.8 | 11396.6 | 10025.8 | 8364.4 |
| **30** | 28958.1 | 26630.6 | 22979.8 | 18697.8 | 14308.1 | -10074.6 | 7699.86 | 4928.26 | 4283.48 | 3033.5 |
| **40** | 37611.1 | 33476.4 | 26873.1 | 19122. | 11454.6 | -31626.5 | 439.89 | -3660.04 | -3784.82 | -4819.4 |
| **50** | 52348.1 | 45648.2 | 34840.4 | 22100.2 | 9667.13 | -58024.4 | -8120.08 | -14368.3 | -14179.1 | -15194.3 |
| **60** | 73169.1 | 63146. | 46881.7 | 27632.4 | 8945.63 | -89268.3 | -17980.1 | -27196.6 | -26899.4 | -28091.2 |
| **70** | 100074. | 85969.8 | 62997. | 35718.6 | 9290.13 | -125358. | -29140. | -42144.9 | -41945.7 | -43510.1 |
| **80** | 133063. | 114120. | 83186.3 | 46358.8 | 10700.6 | -166294. | -41600. | -59213.2 | -59318. | -61451. |
| **90** | 172136. | 147595. | 107450. | 59553. | 13177.1 | -212076. | -55360. | -78401.5 | -79016.3 | -81913.9 |
| **100** | 217293. | 186397. | 135787. | 75301.2 | 16719.6 | -262704. | -70419.9 | -99709.8 | -101041. | -104899. |

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**Table: 2 Case-2 HH Grade, White Matter, 500 cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 493.79 | 475.61 | 446.8 | 409.37 | 365.81 | 318.81 | 270.99 | 224.66 | 181.65 | 143.25 |
| **10** | 340.49 | 330.21 | 312.8 | 289.57 | 261.71 | 236.51 | 205.39 | 175.26 | 148.35 | 122.85 |
| **20** | 305.19 | 288.81 | 262.8 | 229.77 | 191.61 | 168.81 | 133.79 | 103.86 | 85.05 | 70.45 |
| **30** | 387.89 | 351.41 | 296.8 | 229.97 | 155.51 | 115.71 | 56.19 | 10.46 | -8.25 | -13.95 |
| **40** | 588.59 | 518.01 | 414.8 | 290.17 | 153.41 | 77.21 | -27.41 | -104.94 | -131.55 | -130.35 |
| **50** | 907.29 | 788.61 | 616.8 | 410.37 | 185.31 | 53.31 | -117.01 | -242.34 | -284.85 | -278.75 |
| **60** | 1343.99 | 1163.21 | 902.8 | 590.57 | 251.21 | 44.01 | -212.61 | -401.74 | -468.15 | -459.15 |
| **70** | 1898.69 | 1641.81 | 1272.8 | 830.77 | 351.11 | 49.31 | -314.21 | -583.14 | -681.45 | -671.55 |
| **80** | 2571.39 | 2224.41 | 1726.8 | 1130.97 | 485.01 | 69.21 | -421.81 | -786.54 | -924.75 | -915.95 |
| **90** | 3362.09 | 2911.01 | 2264.8 | 1491.17 | 652.91 | 103.71 | -535.41 | -1011.94 | -1198.05 | -1192.35 |
| **100** | 4270.79 | 3701.61 | 2886.8 | 1911.37 | 854.81 | 152.81 | -655.01 | -1259.34 | -1501.35 | -1500.75 |

**Table: 2a Case-2 HH Grade, White Matter, 500 cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 493.79 | 475.61 | 446.8 | 409.37 | 365.81 | 318.81 | 270.99 | 224.66 | 181.65 | 143.25 |
| **10** | 373.79 | 361.21 | 343.2 | 318.97 | 290.21 | 231.11 | 229.09 | 197.06 | 167.56 | 139.45 |
| **20** | 329.79 | 312.81 | 291.6 | 260.57 | 228.01 | 82.81 | 171.19 | 143.46 | 123.47 | 103.65 |
| **30** | 361.79 | 330.41 | 292. | 234.17 | 179.21 | -126.09 | 97.29 | 63.86 | 49.38 | 35.85 |
| **40** | 469.79 | 414.01 | 344.4 | 239.77 | 143.81 | -395.59 | 7.39 | -41.74 | -54.71 | -63.95 |
| **50** | 653.79 | 563.61 | 448.8 | 277.3 | 121.8 | - | -98.51 | - | -188.8 | - |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 7 | 1 | 725.69 | | 173.34 | | 195.75 |
| **60** | 913.79 | 779.21 | 605.2 | 346.97 | 113.21 | -1116.39 | -220.41 | -330.94 | -352.89 | -359.55 |
| **70** | 1249.79 | 1060.81 | 813.6 | 448.57 | 118.01 | -1567.69 | -358.31 | -514.54 | -546.98 | -555.35 |
| **80** | 1661.79 | 1408.41 | 1074. | 582.17 | 136.21 | -2079.59 | -512.21 | -724.14 | -771.07 | -783.15 |
| **90** | 2149.79 | 1822.01 | 1386.4 | 747.77 | 167.81 | -2652.09 | -682.11 | -959.74 | -1025.16 | -1042.95 |
| **100** | 2713.79 | 2301.61 | 1750.8 | 945.37 | 212.81 | -3285.19 | -868.01 | -1221.34 | -1309.25 | -1334.75 |

**Table: 3 Case-2 HH Grade, Gray Matter, 40000 cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| **t** | **x=0.1** | **x=0.2** | **x=0.3** | **x=0.4** | **x=0.5** | **x=0.6** | **x=0.7** | **x=0.8** | **x=0.9** | **x=1** |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39012.4 | 36193.5 | 31940.7 | 26812.8 | 21410.5 | 16262.8 | 11750.3 | 8075.86 | 5279.75 | 3283.4 |
| **10** | 28401.3 | 26457. | 23635.9 | 20217. | 16485.8 | 12945. | 9670.21 | 6937.26 | 4751.45 | 3128.7 |
| **20** | 22316.2 | 20628.5 | 18333.1 | 15659.2 | 12631.1 | 10017.2 | 7566.11 | 5556.66 | 3969.15 | 2704. |
| **30** | 20757.1 | 18708. | 16032.3 | 13139.4 | 9846.36 | 7479.39 | 5438.01 | 3934.06 | 2932.85 | 2009.3 |
| **40** | 23724. | 20695.5 | 16733.4 | 12657.6 | 8131.66 | 5331.59 | 3285.91 | 2069.46 | 1642.55 | 1044.6 |
| **50** | 31216.9 | 26591. | 20436.7 | 14213.8 | 7486.96 | 3573.79 | 1109.81 | -37.14 | 98.25 | -190.1 |
| **60** | 43235.8 | 36394.5 | 27141.9 | 17808. | 7912.26 | 2205.99 | -1090.29 | -2385.74 | -1700.05 | -1694.8 |
| **70** | 59780.7 | 50106. | 36849. | 23440.2 | 9407.56 | 1228.19 | -3314.39 | -4976.34 | -3752.35 | -3469.5 |
| **80** | 80851.6 | 67725.5 | 49558.2 | 31110.4 | 11972.9 | 640.39 | -5562.49 | -7808.94 | -6058.65 | -5514.2 |
| **90** | 106449. | 89253. | 65269.5 | 40818.6 | 15608.2 | 442.59 | -7834.59 | -10883.5 | -8618.95 | -7828.9 |
| **100** | 136571. | 114689. | 83982.7 | 52564.8 | 20313.5 | 634.79 | -10130. | -14200. | -11433. | -10413. |

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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 7 | 1 | 3 | 6 |

**Table: 3a Case-2 HH Grade, Gray Matter, 40000 cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39012.4 | 36193.5 | 31940.7 | 26812.8 | 21410.5 | 16262.8 | 11750.3 | 8075.86 | 5279.75 | 3283.4 |
| **10** | 31248.5 | 29207.9 | 26223.6 | 22388.5 | 21219.9 | 14421.9 | 10786.8 | 7744.36 | 5295.15 | 3490.2 |
| **20** | 25902.6 | 24176.3 | 21912.5 | 18768.2 | 21291.3 | 12477. | 9541.31 | 7072.86 | 5024.55 | 3486.8 |
| **30** | 22974.7 | 21098.7 | 19007.4 | 15951.9 | 21624.7 | 10428.1 | 8013.81 | 6061.36 | 4467.95 | 3273.2 |
| **40** | 22464.8 | 19975.1 | 17508.3 | 13939.6 | 22220.1 | 8275.19 | 6204.31 | 4709.86 | 3625.35 | 2849.4 |
| **50** | 24372.9 | 20805.5 | 17415.2 | 12731.3 | 23077.5 | 6018.29 | 4112.81 | 3018.36 | 2496.75 | 2215.4 |
| **60** | 28699. | 23589.9 | 18728.1 | 12327. | 24196.9 | 3657.39 | 1739.31 | 986.86 | 1082.15 | 1371.2 |
| **70** | 35443.1 | 28328.3 | 21447. | 12726.7 | 25578.3 | 1192.49 | -916.19 | -1384.64 | -618.45 | 316.8 |
| **80** | 44605.2 | 35020.7 | 25571.9 | 13930.4 | 27221.7 | -1376.41 | -3853.69 | -4096.14 | -2605.05 | -947.8 |
| **90** | 56185.3 | 43667.1 | 31102.8 | 15938.1 | 29127.1 | -4049.31 | -7073.19 | -7147.64 | -4877.65 | -2422.6 |
| **100** | 70183.4 | 54267.5 | 38039.7 | 18749.8 | 31294.5 | -6826.21 | -10574.7 | -10539.1 | -7436.25 | -4107.6 |

**Table: 4 Case-2 HH Grade, Gray Matter, 500 cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 487.65 | 452.42 | 399.26 | 335.16 | 267.63 | 203.28 | 146.88 | 100.95 | 65.997 | 41.04 |
| **10** | 354.75 | 330.32 | 295.66 | 252.96 | 206.43 | 161.38 | 120.83 | 86.75 | 59.397 | 39.09 |
| **20** | 277.85 | 256.22 | 230.06 | 196.76 | 159.23 | 123.48 | 94.48 | 69.55 | 49.597 | 33.74 |
| **30** | 256.95 | 230.12 | 202.46 | 166.56 | 126.03 | 89.58 | 67.83 | 49.35 | 36.597 | 24.99 |
| **40** | 292.05 | 252.02 | 212.86 | 162.36 | 106.83 | 59.68 | 40.88 | 26.15 | 20.397 | 12.84 |
| **50** | 383.15 | 321.92 | 261.26 | 184.1 | 101.6 | 33.78 | 13.63 | -0.05 | 0.997 | -2.71 |

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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 6 | 3 | | | | | |
| **60** | 530.25 | 439.82 | 347.66 | 231.96 | 110.43 | 11.88 | -13.92 | -29.25 | -21.603 | -21.66 |
| **70** | 733.35 | 605.72 | 472.06 | 305.76 | 133.23 | -6.02 | -41.77 | -61.45 | -47.403 | -44.01 |
| **80** | 992.45 | 819.62 | 634.46 | 405.56 | 170.03 | -19.92 | -69.92 | -96.65 | -76.403 | -69.76 |
| **90** | 1307.55 | 1081.52 | 834.86 | 531.36 | 220.83 | -29.82 | -98.37 | -134.85 | -108.603 | -98.91 |
| **100** | 1678.65 | 1391.42 | 1073.26 | 683.16 | 285.63 | -35.72 | -127.12 | -176.05 | -144.003 | -131.46 |

**Table: 4a Case-2 HH Grade, Gray Matter, 500 cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| **t** | **x=0.1** | **x=0.2** | **x=0.3** | **x=0.4** | **x=0.5** | **x=0.6** | **x=0.7** | **x=0.8** | **x=0.9** | **x=1** |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 487.65 | 452.42 | 399.26 | 335.16 | 267.63 | 203.28 | 146.88 | 100.95 | 65.997 | 41.04 |
| **10** | 390.45 | 364.92 | 327.96 | 279.86 | 229.53 | 180.23 | 134.78 | 96.831 | 66.177 | 43.64 |
| **20** | 323.25 | 301.42 | 274.66 | 234.56 | 195.43 | 155.88 | 119.08 | 88.512 | 62.757 | 43.64 |
| **30** | 286.05 | 261.92 | 239.36 | 199.26 | 165.33 | 130.23 | 99.78 | 75.993 | 55.737 | 41.04 |
| **40** | 278.85 | 246.42 | 222.06 | 173.96 | 139.23 | 103.28 | 76.88 | 59.274 | 45.117 | 35.84 |
| **50** | 301.65 | 254.92 | 222.76 | 158.66 | 117.13 | 75.03 | 50.38 | 38.355 | 30.897 | 28.04 |
| **60** | 354.45 | 287.42 | 241.46 | 153.36 | 99.03 | 45.48 | 20.28 | 13.236 | 13.077 | 17.64 |
| **70** | 437.25 | 343.92 | 278.16 | 158.06 | 84.93 | 14.63 | -13.42 | -16.083 | -8.343 | 4.64 |
| **80** | 550.05 | 424.42 | 332.86 | 172.76 | 74.83 | -17.52 | -50.72 | -49.602 | -33.363 | -10.96 |
| **90** | 692.85 | 528.92 | 405.56 | 197.46 | 68.73 | -50.97 | -91.62 | -87.321 | -61.983 | -29.16 |
| **100** | 865.65 | 657.42 | 496.26 | 232.16 | 66.63 | -85.72 | -136.12 | -129.24 | -94.203 | -49.96 |

**Graphical Representation:** HH Grade: High $\rho$, High $D$

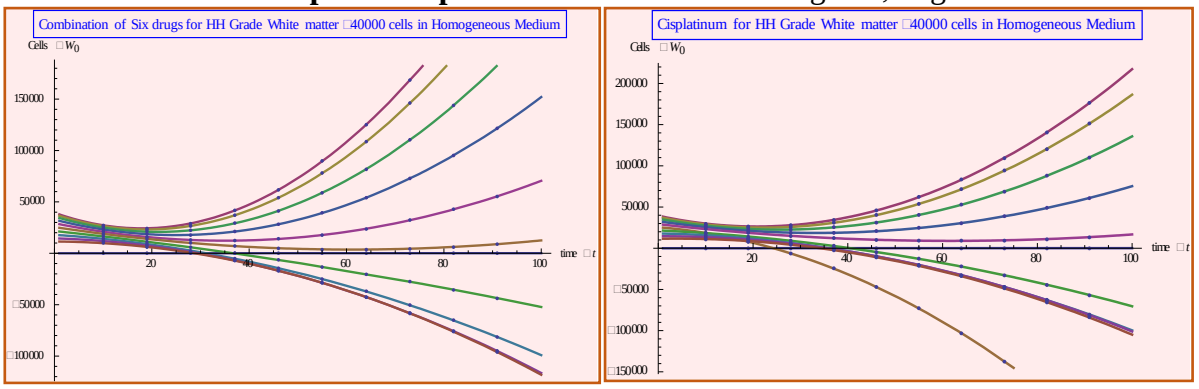

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**Fig. 5 & 5a: HH Grade, White Matter, 40000 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

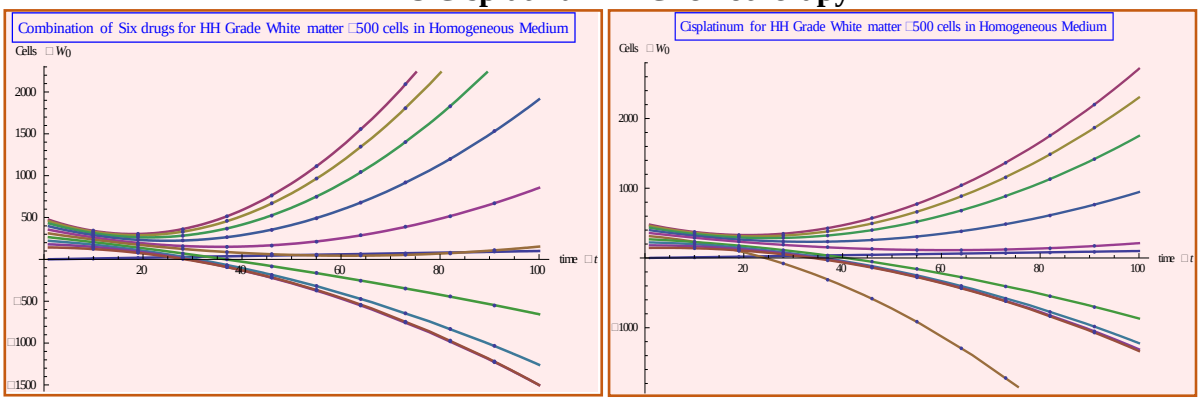


**Fig. 6 & 6a: HH Grade, White Matter, 500 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

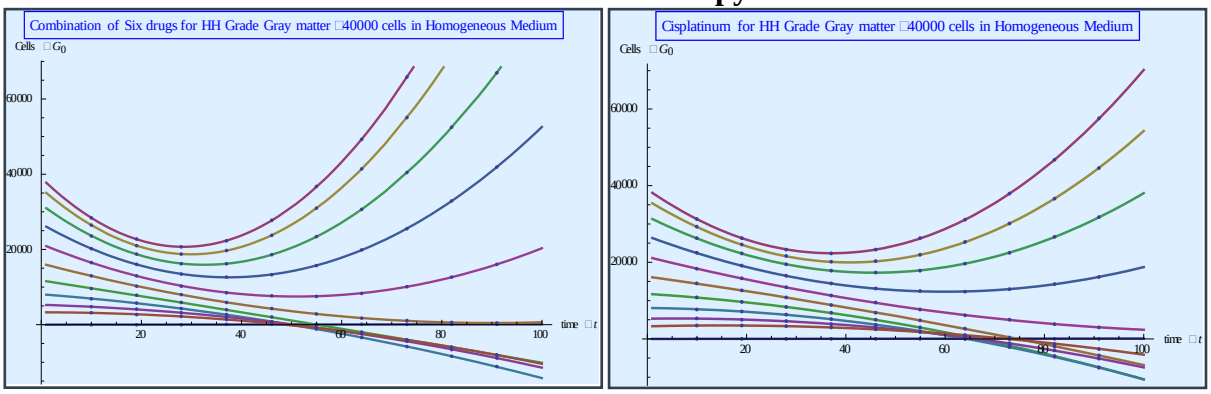


**Fig. 7 & 7a: HH Grade, Gray Matter, 40000 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

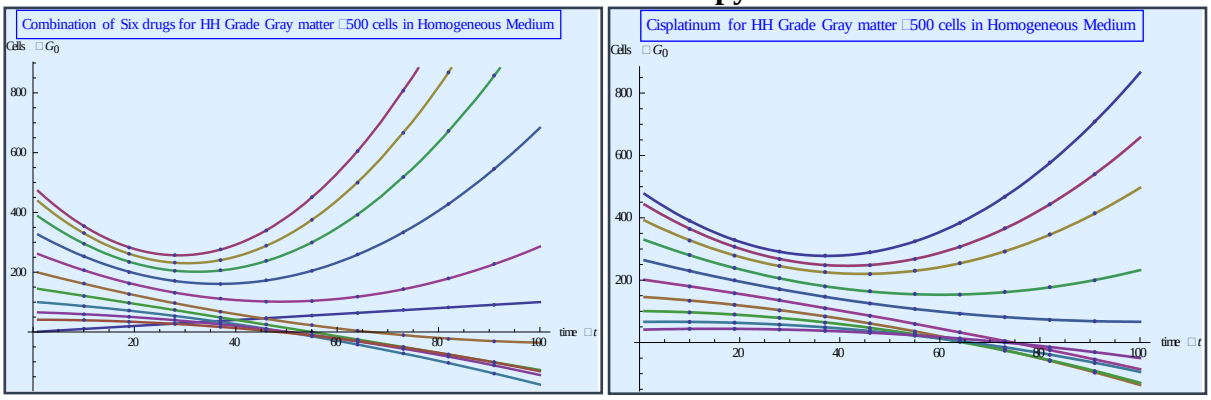


**Fig. 8 & 8a: HH Grade, Gray Matter, 500 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

**Numerical Parameters:** For HL Grade (High $\rho$, Low $D$)

| **Parameters** | **White Matter** | **Gray Matter** |
|---|---|---|
| Velocity of Cells | $v_W = 0.00088\ cm/day$ | $v_G = 0.0004\ cm/day$ |
| Diffusion Rate | $D_W = 0.000016\ cm^2/day$ | $D_G = 0.0000033\ cm^2/day$ |
| Growth Rate | $\rho_W = 0.012\ cm/day$ [9,10] | $\rho_G = 0.012\ cm/day$ [9,10] |

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| | | |
|---|---|---|
| Number of Cells | $W_0 = a = 40000$ & 500 | $G_0 = c = 40000$ & 500 |
| Measure of spread of tumor cells | $b = 0.8\,\text{cm}$ | $d = 0.4\,\text{cm}$ |
| Centre | $x_0 = 0$ | $x_0 = 0$ |
| $K_1$ - Combination of Six Drugs | 0.0391 [9,10] | 0.0391 [9,10] |
| $K_2$ -Cisplatinum | 0.0285 [9,10] | 0.0285 [9,10] |

**Table: 5 Case-2 HL Grade, White Matter, 40000 cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39503.1 | 38049.2 | 35743.9 | 32749.2 | 29264.6 | 25505.1 | 21679.8 | 17973.2 | 14532.4 | 11460.2 |
| **10** | 30259.3 | 29145.9 | 27380. | 25085.9 | 22417.1 | 19536.7 | 16606.3 | 13767.4 | 11131.7 | 8778.9 |
| **20** | 23859.5 | 22982.6 | 21590.1 | 19780.6 | 17677.6 | 15404.3 | 13092.8 | 10855.6 | 8776.98 | 6923.6 |
| **30** | 20303.7 | 19559.3 | 18374.2 | 16833.3 | 15046.1 | 13107.9 | 11139.3 | 9237.76 | 7468.28 | 5894.3 |
| **40** | 19591.9 | 18876. | 17732.3 | 16244. | 14522.6 | 12647.5 | 10745.8 | 8913.96 | 7205.58 | 5691. |
| **50** | 21724.1 | 20932.7 | 19664.4 | 18012.7 | 16107.1 | 14023.1 | 11912.3 | 9884.16 | 7988.88 | 6313.7 |
| **60** | 26700.3 | 25729.4 | 24170.5 | 22139.4 | 19799.6 | 17234.7 | 14638.8 | 12148.4 | 9818.18 | 7762.4 |
| **70** | 34520.5 | 33266.1 | 31250.6 | 28624.1 | 25600.1 | 22282.3 | 18925.3 | 15706.6 | 12693.5 | 10037.1 |
| **80** | 45184.7 | 43542.8 | 40904.7 | 37466.8 | 33508.6 | 29165.9 | 24771.8 | 20558.8 | 16614.8 | 13137.8 |
| **90** | 58692.9 | 56559.5 | 53132.8 | 48667.5 | 43525.1 | 37885.5 | 32178.3 | 26705. | 21582.1 | 17064.5 |
| **100** | 75045.1 | 72316.2 | 67934.9 | 62226.2 | 55649.6 | 48441.1 | 41144.8 | 34145.2 | 27595.4 | 21817.2 |

**Table: 5a Case-2 HL Grade, White Matter, 40000 Cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39503.1 | 38049.2 | 35743.9 | 32749.2 | 29264.6 | 25505.1 | 21679.8 | 17973.2 | 14532.4 | 11460.2 |
| **10** | 33340.6 | 32113.8 | 30167.4 | 27639.8 | 24699.6 | 21526.2 | 18298.2 | 15169.8 | 12264.9 | 9672. |
| **20** | 28284.1 | 27244.4 | 25590.9 | 23446.4 | 20954.6 | 18261.3 | 15524.6 | 12870.4 | 10403.4 | 8203.8 |
| **30** | 24333.6 | 23441. | 22014.4 | 20169. | 18029.6 | 15710.4 | 13359. | 11075. | 8947.88 | 7055.6 |
| **40** | 21489. | 20703. | 19437. | 17807. | 15924. | 13873. | 11801. | 9783.5 | 7898.3 | 6227.4 |

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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 6 | 9 | 6 | 6 | 5 | 4 | 6 | 8 | |
| **50** | 19750.6 | 19032.2 | 17861.4 | 16362.2 | 14639.6 | 12750.6 | 10851.8 | 8996.16 | 7254.88 | 5719.2 |
| **60** | 19118.1 | 18426.8 | 17284.9 | 15832.8 | 14174.6 | 12341.7 | 10510.2 | 8712.76 | 7017.38 | 5531. |
| **70** | 19591.6 | 18887.4 | 17708.4 | 16219.4 | 14529.6 | 12646.8 | 10776.6 | 8933.36 | 7185.88 | 5662.8 |
| **80** | 21171.1 | 20414. | 19131.9 | 17522. | 15704.6 | 13665.9 | 11651. | 9657.96 | 7760.38 | 6114.6 |
| **90** | 23856.6 | 23006.6 | 21555.4 | 19740.6 | 17699.6 | 15399. | 13133.4 | 10886.6 | 8740.88 | 6886.4 |
| **100** | 27648.1 | 26665.2 | 24978.9 | 22875.2 | 20514.6 | 17846.1 | 15223.8 | 12619.2 | 10127.4 | 7978.2 |

**Table: 6 Case-2 HL Grade, White Matter, 500 Cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 493.79 | 475.61 | 446.8 | 409.37 | 365.81 | 318.81 | 270.99 | 224.66 | 181.65 | 143.25 |
| **10** | 378.49 | 364.21 | 342.2 | 313.87 | 280.01 | 243.71 | 207.79 | 171.96 | 139.65 | 109.55 |
| **20** | 299.19 | 286.81 | 269.6 | 248.37 | 220.21 | 190.61 | 164.59 | 135.26 | 111.65 | 85.85 |
| **30** | 255.89 | 243.41 | 229. | 212.87 | 186.41 | 159.51 | 141.39 | 114.56 | 97.65 | 72.15 |
| **40** | 248.59 | 234.01 | 220.4 | 207.37 | 178.61 | 150.41 | 138.19 | 109.86 | 97.65 | 68.45 |
| **50** | 277.29 | 258.61 | 243.8 | 231.87 | 196.81 | 163.31 | 154.99 | 121.16 | 111.65 | 74.75 |
| **60** | 341.99 | 317.21 | 299.2 | 286.37 | 241.01 | 198.21 | 191.79 | 148.46 | 139.65 | 91.05 |
| **70** | 442.69 | 409.81 | 386.6 | 370.87 | 311.21 | 255.11 | 248.59 | 191.76 | 181.65 | 117.35 |
| **80** | 579.39 | 536.41 | 506. | 485.37 | 407.41 | 334.01 | 325.39 | 251.06 | 237.65 | 153.65 |
| **90** | 752.09 | 697.01 | 657.4 | 629.87 | 529.61 | 434.91 | 422.19 | 326.36 | 307.65 | 199.95 |
| **100** | 960.79 | 891.61 | 840.8 | 804.37 | 677.81 | 557.81 | 538.99 | 417.66 | 391.65 | 256.25 |

**Table: 6a Case-2 HL Grade, White Matter, 500 Cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 493.79 | 475.61 | 446.8 | 409.37 | 365.81 | 318.81 | 270.99 | 224.66 | 181.65 | 143.25 |
| **10** | 416.79 | 401.41 | 377.1 | 345.47 | 308.71 | 269.11 | 228.69 | 189.56 | 153.25 | 120.85 |
| **20** | 353.59 | 340.61 | 320. | 292.97 | 261.81 | 228.41 | 193.99 | 160.66 | 129.85 | 102.45 |
| **30** | 304.19 | 293.21 | 275.5 | 251.87 | 225.11 | 196.71 | 166.89 | 137.96 | 111.45 | 88.05 |
| **40** | 268.59 | 259.21 | 243.6 | 222.17 | 198.61 | 174.01 | 147.39 | 121.46 | 98.05 | 77.65 |
| **50** | 246.79 | 238.61 | 224.3 | 203.87 | 182.31 | 160.31 | 135.49 | 111.16 | 89.65 | 71.25 |
| **60** | 238.79 | 231.41 | 217.6 | 196.97 | 176.21 | 155.61 | 131.19 | 107.06 | 86.25 | 68.85 |
| **70** | 244.59 | 237.61 | 223.5 | 201.47 | 180.31 | 159.91 | 134.49 | 109.16 | 87.85 | 70.45 |
| **80** | 264.19 | 257.21 | 242. | 217.37 | 194.61 | 173.21 | 145.39 | 117.46 | 94.45 | 76.05 |
| **90** | 297.59 | 290.21 | 273.1 | 244.67 | 219.11 | 195.51 | 163.89 | 131.96 | 106.05 | 85.65 |
| **100** | 344.79 | 336.61 | 316.8 | 283.37 | 253.81 | 226.81 | 189.99 | 152.66 | 122.65 | 99.25 |

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**Table: 7 Case-2 HL Grade, Gray Matter, 40000 Cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39012.4 | 36193.5 | 31940.7 | 26812.8 | 21410.5 | 16262.8 | 11750.3 | 8075.86 | 5279.75 | 3283.4 |
| **10** | 29883.1 | 27724.3 | 24466.7 | 20538.3 | 16400.7 | 12456.8 | 9000.71 | 6186.36 | 4044.25 | 2514.9 |
| **20** | 23561.8 | 21861.1 | 19292.7 | 16193.8 | 12932.9 | 9820.79 | 7097.11 | 4878.86 | 3188.75 | 1982.4 |
| **30** | 20048.5 | 18603.9 | 16418.7 | 13779.3 | 11007.1 | 8354.79 | 6039.51 | 4153.36 | 2713.25 | 1685.9 |
| **40** | 19343.2 | 17952.7 | 15844.7 | 13294.8 | 10623.3 | 8058.79 | 5827.91 | 4009.86 | 2617.75 | 1625.4 |
| **50** | 21445.9 | 19907.5 | 17570.7 | 14740.3 | 11781.5 | 8932.79 | 6462.31 | 4448.36 | 2902.25 | 1800.9 |
| **60** | 26356.6 | 24468.3 | 21596.7 | 18115.8 | 14481.7 | 10976.8 | 7942.71 | 5468.86 | 3566.75 | 2212.4 |
| **70** | 34075.3 | 31635.1 | 27922.7 | 23421.3 | 18723.9 | 14190.8 | 10269.1 | 7071.36 | 4611.25 | 2859.9 |
| **80** | 44602. | 41407.9 | 36548.7 | 30656.8 | 24508.1 | 18574.8 | 13441.5 | 9255.86 | 6035.75 | 3743.4 |
| **90** | 57936.7 | 53786.7 | 47474.7 | 39822.3 | 31834.3 | 24128.8 | 17459.9 | 12022.4 | 7840.25 | 4862.9 |
| **100** | 74079.4 | 68771.5 | 60700.7 | 50917.8 | 40702.5 | 30852.8 | 22324.3 | 15370.9 | 10024.7 | 6218.4 |

**Table: 7a Case-2 HL Grade, Gray Matter, 40000 Cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39012.4 | 36193.5 | 31940.7 | 26812.8 | 21410.5 | 16262.8 | 11750.3 | 8075.86 | 5279.75 | 3283.4 |
| **10** | 32926.3 | 30547.6 | 26957.8 | 22629.6 | 18070.4 | 13726.1 | 9917.71 | 6815.96 | 4456.15 | 2771.2 |
| **20** | 27932.2 | 25915.7 | 22868.9 | 19196.4 | 15329.7 | 11645.4 | 8415.11 | 5782.06 | 3780.55 | 2351. |
| **30** | 24030.1 | 22297.8 | 19674. | 16513.2 | 13188.4 | 10020.7 | 7242.51 | 4974.16 | 3252.95 | 2022.8 |
| **40** | 21220. | 19693.9 | 17373.1 | 14580. | 11646.5 | 8851.99 | 6399.91 | 4392.26 | 2873.35 | 1786.6 |
| **50** | 19501.9 | 18104. | 15966.2 | 13396.8 | 10704. | 8139.29 | 5887.31 | 4036.36 | 2641.75 | 1642.4 |
| **60** | 18875.8 | 17528.1 | 15453.3 | 12963.6 | 10360.9 | 7882.59 | 5704.71 | 3906.46 | 2558.15 | 1590.2 |
| **70** | 19341.7 | 17966.2 | 15834.3 | 13280.4 | 10617.2 | 8081.89 | 5852.11 | 4002.56 | 2622.55 | 1630. |
| **80** | 20899. | 19418. | 17109. | 14347. | 11472. | 8737.1 | 6329.5 | 4324.6 | 2834.9 | 1761. |

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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 6 | 3 | 5 | 2 | 9 | 9 | 1 | 6 | 5 | 8 |
| **90** | 23549.5 | 21884.4 | 19278.6 | 16164. | 12928. | 9848.49 | 7136.91 | 4872.76 | 3195.35 | 1985.6 |
| **100** | 27291.4 | 25364.5 | 22341.7 | 18730.8 | 14982.5 | 11415.8 | 8274.31 | 5646.86 | 3703.75 | 2301.4 |

**Table: 8 Case-2 HL Grade, Gray Matter, 500 Cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 487.65 | 452.42 | 399.26 | 335.16 | 267.63 | 203.28 | 146.88 | 100.95 | 65.997 | 41.04 |
| **10** | 373.95 | 346.22 | 305.46 | 256.66 | 205.33 | 155.38 | 112.18 | 77.65 | 50.197 | 30.94 |
| **20** | 296.25 | 272.02 | 239.66 | 202.16 | 163.03 | 121.48 | 87.48 | 62.35 | 38.397 | 22.84 |
| **30** | 254.55 | 229.82 | 201.86 | 171.66 | 140.73 | 101.58 | 72.78 | 55.05 | 30.597 | 16.74 |
| **40** | 248.85 | 219.62 | 192.06 | 165.16 | 138.43 | 95.68 | 68.08 | 55.75 | 26.797 | 12.64 |
| **50** | 279.15 | 241.42 | 210.26 | 182.66 | 156.13 | 103.78 | 73.38 | 64.45 | 26.997 | 10.54 |
| **60** | 345.45 | 295.22 | 256.46 | 224.16 | 193.83 | 125.88 | 88.68 | 81.15 | 31.197 | 10.44 |
| **70** | 447.75 | 381.02 | 330.66 | 289.66 | 251.53 | 161.98 | 113.98 | 105.85 | 39.397 | 12.34 |
| **80** | 586.05 | 498.82 | 432.86 | 379.16 | 329.23 | 212.08 | 149.28 | 138.55 | 51.597 | 16.24 |
| **90** | 760.35 | 648.62 | 563.06 | 492.66 | 426.93 | 276.18 | 194.58 | 179.25 | 67.797 | 22.14 |
| **100** | 970.65 | 830.42 | 721.26 | 630.16 | 544.63 | 354.28 | 249.88 | 227.95 | 87.997 | 30.04 |

**Table: 8a Case-2 HL Grade, Gray Matter, 500 Cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 487.65 | 452.42 | 399.26 | 335.16 | 267.63 | 203.28 | 146.88 | 100.95 | 65.997 | 41.04 |
| **10** | 411.55 | 381.82 | 336.96 | 282.86 | 225.83 | 171.48 | 124.01 | 85.15 | 55.697 | 34.66 |
| **20** | 349.05 | 323.82 | 285.86 | 239.96 | 191.43 | 145.28 | 105.34 | 72.15 | 47.197 | 29.48 |
| **30** | 300.15 | 278.42 | 245.96 | 206.46 | 164.43 | 124.68 | 90.87 | 61.95 | 40.497 | 25.5 |
| **40** | 264.85 | 245.62 | 217.26 | 182.36 | 144.83 | 109.68 | 80.6 | 54.55 | 35.597 | 22.72 |
| **50** | 243.15 | 225.42 | 199.76 | 167.66 | 132.63 | 100.28 | 74.53 | 49.95 | 32.497 | 21.14 |
| **60** | 235.05 | 217.82 | 193.46 | 162.36 | 127.83 | 96.48 | 72.66 | 48.15 | 31.197 | 20.76 |
| **70** | 240.55 | 222.82 | 198.36 | 166.46 | 130.43 | 98.28 | 74.99 | 49.15 | 31.697 | 21.58 |
| **80** | 259.65 | 240.42 | 214.46 | 179.96 | 140.43 | 105.68 | 81.52 | 52.95 | 33.997 | 23.6 |
| **90** | 292.35 | 270.62 | 241.76 | 202.86 | 157.83 | 118.68 | 92.25 | 59.55 | 38.097 | 26.82 |
| **100** | 338.65 | 313.42 | 280.26 | 235.16 | 182.63 | 137.28 | 107.18 | 68.95 | 43.997 | 31.24 |

**Graphical Representation:** HL Grade: High $\rho$, Low $D$

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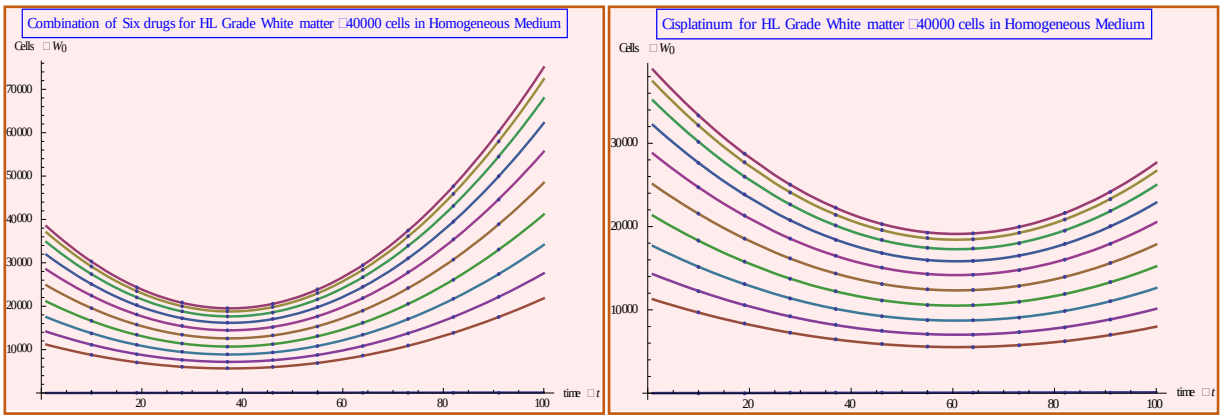


**Fig. 9 & 9a: HL Grade, White Matter, 40000 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

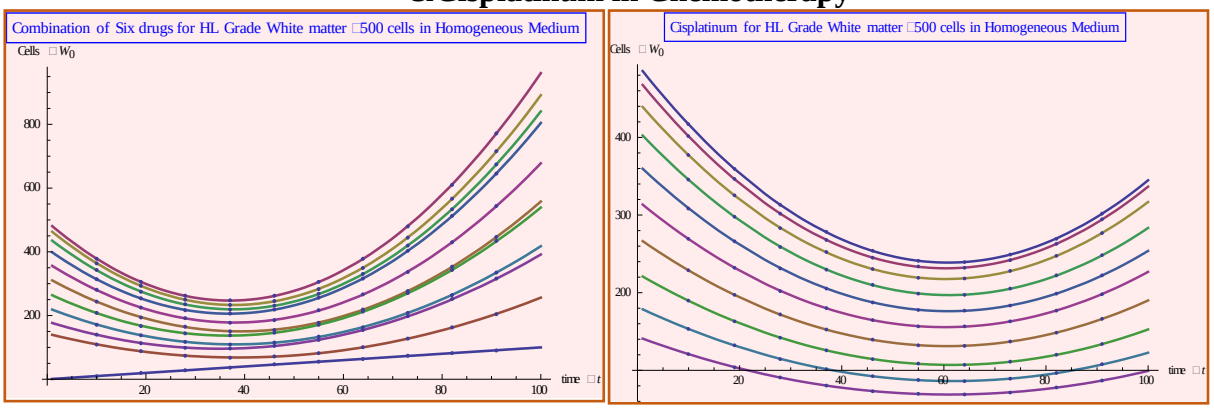


**Fig. 10 & 10a: HL Grade, White Matter, 500 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

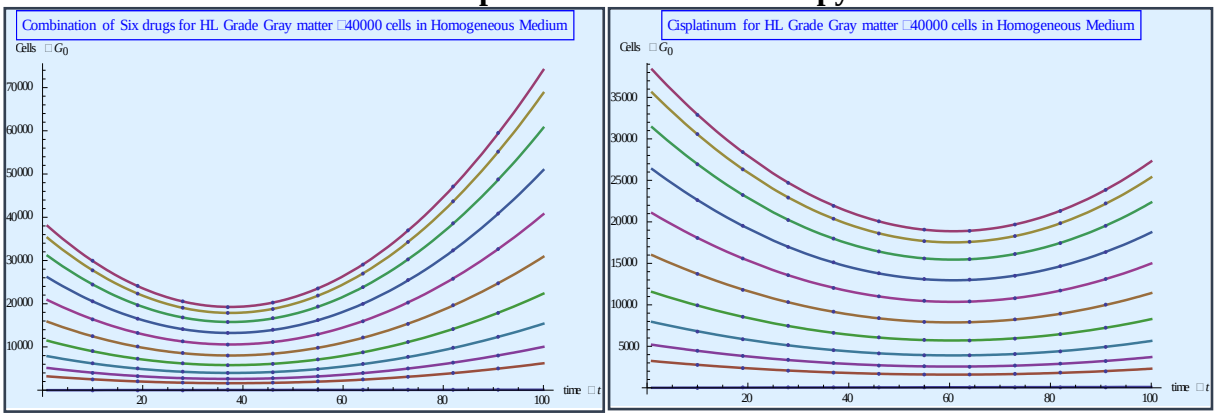


**Fig. 11 & 11a: HL Grade, Gray Matter, 40000 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

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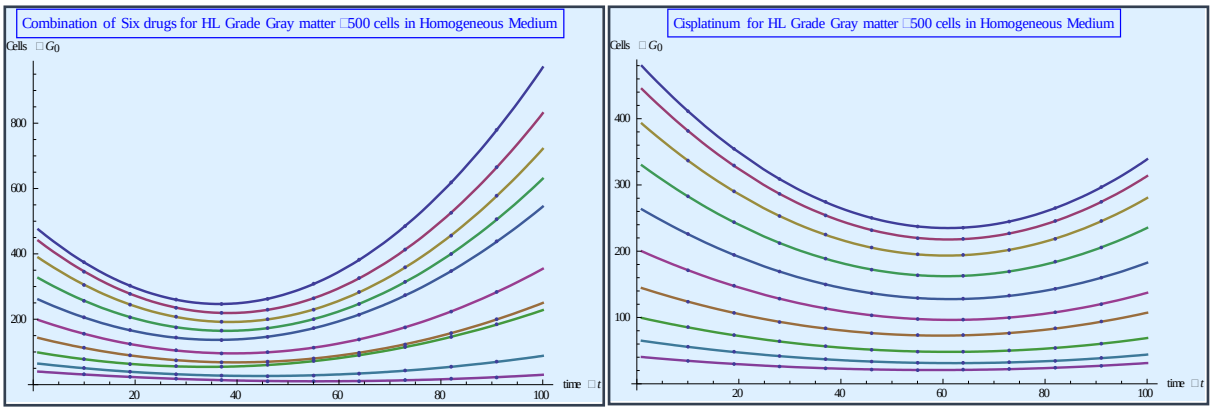


**Fig. 12 & 12a: HL Grade, Gray Matter, 500 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

**Numerical Parameters:** For LH Grade (Low $\rho$, High $D$)

| **Parameters** | **White Matter** | **Gray Matter** |
|---|---|---|
| Velocity of Cells | $v_W = 0.018\ cm/day_{[9,10]}$ | $v_G = 0.008\ cm/day_{[9,10]}$ |
| Diffusion Rate | $D_W = 0.0065\ cm^2/day_{[9,10]}$ | $D_G = 0.0013\ cm^2/day_{[9,10]}$ |
| Growth Rate | $\rho_W = 0.008\ cm/day_{[9,10]}$ | $\rho_G = 0.008\ cm/day_{[9,10]}$ |
| Number of Cells | $W_0 = a = 40000$ & 500 | $G_0 = c = 40000$ & 500 |
| Measure of spread of tumor cells | $b = 0.8$ cm | $d = 0.4$ cm |
| Centre | $x_0 = 0$ | $x_0 = 0$ |
| $K_1$ | 0.0391 [9,10] | 0.0391 [9,10] |

**Table: 9 Case-2 LH Grade, White Matter, 40000 Cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| **t** | **x=0.1** | **x=0.2** | **x=0.3** | **x=0.4** | **x=0.5** | **x=0.6** | **x=0.7** | **x=0.8** | **x=0.9** | **x=1** |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39503.1 | 38049.2 | 35743.9 | 32749.2 | 29264.6 | 25505.1 | 21679.8 | 17973.2 | 14532.4 | 11460.2 |
| **10** | 103894. | 100830. | 95436. | 88095. | 76965.7 | 68353.5 | 59186.3 | 50144.8 | 40109.9 | 32432. |
| **20** | 334198. | 323417. | 305252. | 280987. | 241725. | 213222. | 183413. | 154208. | 120911. | 96951.8 |
| **30** | 730417. | 705810. | 665192. | 611425. | 523542. | 460110. | 394359. | 330164. | 256937. | 205020. |
| **40** | 1.29255*10^6 | 1.24801*10^6 | 1.17526*10^6 | 1.07941*10^6 | 922417. | 809019. | 692026. | 578012. | 448186. | 356635. |
| **50** | 2.0206*10^6 | 1.95001*10^6 | 1.83544*10^6 | 1.68494*10^6 | 1.43835*10^6 | 1.25995*10^6 | 1.07641*10^6 | 897751. | 694660. | 551799. |
| **60** | 2.91456*10^6 | 2.81182*10^6 | 2.64576*10^6 | 2.42801*10^6 | 2.07134*10^6 | 1.8129*10^6 | 1.54752*10^6 | 1.28938*10^6 | 996357. | 790511. |

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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **70** | 3.97443*10^6 | 3.83344*10^6 | 3.60619*10^6 | 3.30864*10^6 | 2.82139*10^6 | 2.46786*10^6 | 2.10535*10^6 | 1.75291*10^6 | 1.35328*10^6 | 1.07277*10^6 |
| **80** | 5.20022*10^6 | 5.01486*10^6 | 4.71675*10^6 | 4.3268*10^6 | 3.6885*10^6 | 3.22485*10^6 | 2.74989*10^6 | 2.28832*10^6 | 1.76542*10^6 | 1.39858*10^6 |
| **90** | 6.59192*10^6 | 6.35609*10^6 | 5.97744*10^6 | 5.48252*10^6 | 4.67266*10^6 | 4.08386*10^6 | 3.48116*10^6 | 2.89563*10^6 | 2.23279*10^6 | 1.76793*10^6 |
| **100** | 8.14954*10^6 | 7.85713*10^6 | 7.38824*10^6 | 6.77578*10^6 | 5.77389*10^6 | 5.04489*10^6 | 4.29914*10^6 | 3.57483*10^6 | 2.75539*10^6 | 2.18084*10^6 |

**Table: 9a Case-2 LH Grade, White Matter, 40000 Cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| **t** | **x=0.1** | **x=0.2** | **x=0.3** | **x=0.4** | **x=0.5** | **x=0.6** | **x=0.7** | **x=0.8** | **x=0.9** | **x=1** |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39503.1 | 38049.2 | 35743.9 | 32749.2 | 29264.6 | 25505.1 | 21679.8 | 17973.2 | 14532.4 | 11460.2 |
| **10** | 28481.9 | 27890. | 26414.4 | 24233.9 | 22182.1 | 20098. | 17474.2 | 15007.2 | 12788.1 | 10657.6 |
| **20** | 24650.7 | 24046.8 | 22016.9 | 18992.6 | 16737.6 | 15098.9 | 12228.6 | 10063.2 | 8717.78 | 7333. |
| **30** | 28009.5 | 26519.6 | 22551.4 | 17025.3 | 12931.1 | 10507.8 | 5942.97 | 3141.16 | 2321.48 | 1486.4 |
| **40** | 38558.3 | 35308.4 | 28017.9 | 18332. | 10762.6 | 6324.73 | -1382.63 | -5758.84 | -6400.82 | -6882.2 |
| **50** | 56297.1 | 50413.2 | 38416.4 | 22912.7 | 10232.1 | 2549.63 | -9748.23 | -16636.8 | -17449.1 | -17772.8 |
| **60** | 81225.9 | 71834. | 53746.9 | 30767.4 | 11339.6 | -817.47 | -19153.8 | -29492.8 | -30823.4 | -31185.4 |
| **70** | 113345. | 99570.8 | 74009.4 | 41896.1 | 14085.1 | -3776.57 | -29599.4 | -44326.8 | -46523.7 | -47120. |
| **80** | 152654. | 133624. | 99203.9 | 56298.8 | 18468.6 | -6327.67 | -41085. | -61138.8 | -64550. | -65576.6 |
| **90** | 199152. | 173992. | 129330. | 73975.5 | 24490.1 | -8470.77 | -53610.6 | -79928.8 | -84902.3 | -86555.2 |
| **100** | 252841. | 220677. | 164389. | 94926.2 | 32149.6 | -10205.9 | -67176.2 | -100697. | -107581. | -110056. |

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**Table: 10 Case-2 LH Grade, White Matter, 500 Cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 493.79 | 475.61 | 446.8 | 409.37 | 365.81 | 318.81 | 270.99 | 224.66 | 181.65 | 143.25 |
| **10** | 1298.69 | 1260.61 | 1192.7 | 1101.57 | 962.51 | 854.81 | 739.79 | 626.46 | 501.25 | 405.25 |
| **20** | 4177.59 | 4043.61 | 3814.6 | 3513.77 | 3023.21 | 2666.81 | 2292.59 | 1926.26 | 1510.85 | 1211.25 |
| **30** | 9130.49 | 8824.61 | 8312.5 | 7645.97 | 6547.91 | 5754.81 | 4929.39 | 4124.06 | 3210.45 | 2561.25 |
| **40** | 16157.4 | 15603.6 | 14686.4 | 13498.2 | 11536.6 | 10118.8 | 8650.19 | 7219.86 | 5600.05 | 4455.25 |
| **50** | 25258.3 | 24380.6 | 22936.3 | 21070.4 | 17989.3 | 15758.8 | 13455. | 11213.7 | 8679.65 | 6893.25 |
| **60** | 36433.2 | 35155.6 | 33062.2 | 30362.6 | 25906. | 22674.8 | 19343.8 | 16105.5 | 12449.3 | 9875.25 |
| **70** | 49682.1 | 47928.6 | 45064.1 | 41374.8 | 35286.7 | 30866.8 | 26316.6 | 21895.3 | 16908.9 | 13401.3 |
| **80** | 65005. | 62699.6 | 58942. | 54107. | 46131.4 | 40334.8 | 34373.4 | 28583.1 | 22058.5 | 17471.3 |
| **90** | 82401.9 | 79468.6 | 74695.9 | 68559.2 | 58440.1 | 51078.8 | 43514.2 | 36168.9 | 27898.1 | 22085.3 |
| **100** | 101873. | 98235.6 | 92325.8 | 84731.4 | 72212.8 | 63098.8 | 53739. | 44652.7 | 34427.7 | 27243.3 |

**Table: 10a Case-2 LH Grade, White Matter, 500 Cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 493.79 | 475.61 | 446.8 | 409.37 | 365.81 | 318.81 | 270.99 | 224.66 | 181.65 | 143.25 |
| **10** | 356.09 | 348.11 | 330.4 | 303.47 | 277.25 | 251.31 | 218.39 | 187.56 | 159.35 | 132.95 |
| **20** | 308.39 | 298.61 | 276. | 239.57 | 209.17 | 189.01 | 152.79 | 125.66 | 107.05 | 90.65 |
| **30** | 350.69 | 327.11 | 283.6 | 217.67 | 161.57 | 131.91 | 74.19 | 38.96 | 24.75 | 16.35 |
| **40** | 482.99 | 433.61 | 353.2 | 237.77 | 134.45 | 80.01 | -17.41 | -72.54 | -87.55 | -89.95 |
| **50** | 705.29 | 618.11 | 484.8 | 299.87 | 127.81 | 33.31 | -122.01 | -208.84 | -229.85 | -228.25 |
| **60** | 1017.59 | 880.61 | 678.4 | 403.97 | 141.65 | -8.19 | -239.61 | -369.94 | -402.15 | -398.55 |
| **70** | 1419.89 | 1221.11 | 934. | 550.07 | 175.97 | -44.49 | -370.2 | -555.84 | -604.45 | -600.85 |

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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 1 | | | |
| **80** | 1912.19 | 1639.61 | 1251.6 | 738.17 | 230.77 | -75.59 | -513.81 | -766.54 | -836.75 | -835.15 |
| **90** | 2494.49 | 2136.11 | 1631.2 | 968.27 | 306.05 | -101.49 | -670.41 | -1002.04 | -1099.05 | -1101.45 |
| **100** | 3166.79 | 2710.61 | 2072.8 | 1240.37 | 401.81 | -122.19 | -840.01 | -1262.34 | -1391.35 | -1399.75 |

**Table: 11 Case-2 LH Grade, Gray Matter, 40000 Cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| **t** | **x=0.1** | **x=0.2** | **x=0.3** | **x=0.4** | **x=0.5** | **x=0.6** | **x=0.7** | **x=0.8** | **x=0.9** | **x=1** |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39012.4 | 36193.5 | 31940.7 | 26812.8 | 21410.5 | 16262.8 | 11750.3 | 8075.86 | 5279.75 | 3283.4 |
| **10** | 26996.7 | 25226.9 | 22677.5 | 19305.6 | 15758.4 | 12376.5 | 9247.21 | 6629.96 | 4535.15 | 2988.2 |
| **20** | 20599. | 19110.3 | 17246.3 | 14480.4 | 11648.3 | 9174.19 | 6908.11 | 5038.06 | 3568.55 | 2431. |
| **30** | 19819.3 | 17843.7 | 15647. | 12337.2 | 9080.16 | 6655.89 | 4733.01 | 3300.16 | 2379.95 | 1611.8 |
| **40** | 24657.6 | 21427.1 | 17879.9 | 12876. | 8054.06 | 4821.59 | 2721.91 | 1416.26 | 969.35 | 530.6 |
| **50** | 35113.9 | 29860.5 | 23944.7 | 16096.8 | 8569.96 | 3671.29 | 874.81 | -613.64 | -663.25 | -812.6 |
| **60** | 51188.2 | 43143.9 | 33841.4 | 21999.6 | 10627.9 | 3204.99 | -808.29 | -2789.54 | -2517.85 | -2417.8 |
| **70** | 72880.5 | 61277.3 | 47570.2 | 30584.4 | 14227.8 | 3422.69 | -2327.39 | -5111.44 | -4594.45 | -4285. |
| **80** | 100191. | 84260.7 | 65131. | 41851.2 | 19369.7 | 4324.39 | -3682.49 | -7579.34 | -6893.05 | -6414.2 |
| **90** | 133119. | 112094. | 86523.9 | 55800. | 26053.6 | 5910.09 | -4873.59 | -10193.2 | -9413.65 | -8805.4 |
| **100** | 171665. | 144778. | 111749. | 72430.8 | 34279.5 | 8179.79 | -5900.69 | -12953.1 | -12156.3 | -11458.6 |

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**Table: 11a Case-2 LH Grade, Gray Matter, 40000 Cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 39012. | 36193. | 31940.7 | 26812.8 | 21410.5 | 16262.8 | 11750.3 | 8075.86 | 5279.75 | 3283.4 |
| **10** | 31209.7 | 29135.7 | 26414.9 | 22281. | 18156.5 | 14314.4 | 10692.8 | 7664.26 | 5223.55 | 3457.42 |
| **20** | 28869.4 | 26784.4 | 25169.1 | 20483.2 | 16530.5 | 13348. | 10105.3 | 7398.66 | 5160.55 | 3585.48 |
| **30** | 31991.1 | 29139.1 | 28203.3 | 21419.4 | 16532.5 | 13363.6 | 9987.81 | 7279.06 | 5090.75 | 3667.58 |
| **40** | 40574.8 | 36199.8 | 35517.5 | 25089.6 | 18162.5 | 14361.2 | 10340.3 | 7305.46 | 5014.15 | 3703.72 |
| **50** | 54620.5 | 47966.5 | 47111.7 | 31493.8 | 21420.5 | 16340.8 | 11162.8 | 7477.86 | 4930.75 | 3693.9 |
| **60** | 74128.2 | 64439.2 | 62985.9 | 40632. | 26306.5 | 19302.4 | 12455.3 | 7796.26 | 4840.55 | 3638.12 |
| **70** | 99097.9 | 85617.9 | 83140. | 52504.2 | 32820.5 | 23246. | 14217.8 | 8260.66 | 4743.55 | 3536.38 |
| **80** | 129530. | 111503. | 107574. | 67110.4 | 40962.5 | 28171.6 | 16450.3 | 8871.06 | 4639.75 | 3388.68 |
| **90** | 165423. | 142093. | 136288. | 84450.6 | 50732.5 | 34079.2 | 19152.8 | 9627.46 | 4529.15 | 3195.02 |
| **100** | 206779. | 177390. | 169283. | 104525. | 62130.5 | 40968.8 | 22325.3 | 10529.9 | 4411.75 | 2955.4 |

**Table: 12 Case-2 LH Grade, Gray Matter, 500 Cells, Combination of Six Drugs in Chemotherapy, Homogeneous Medium**

| t | x=0.1 | x=0.2 | x=0.3 | x=0.4 | x=0.5 | x=0.6 | x=0.7 | x=0.8 | x=0.9 | x=1 |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 487.65 | 452.42 | 399.26 | 335.16 | 267.63 | 203.28 | 146.88 | 100.95 | 65.997 | 41.04 |
| **10** | 337.35 | 315.02 | 283.56 | 241.56 | 197.33 | 154.38 | 115.58 | 82.84 | 56.797 | 37.34 |
| **20** | 257.05 | 237.62 | 215.86 | 181.96 | 147.03 | 113.48 | 86.28 | 62.91 | 44.997 | 30.44 |
| **30** | 246.75 | 220.22 | 196.16 | 156.36 | 116.73 | 80.58 | 58.98 | 41.16 | 30.597 | 20.34 |
| **40** | 306.45 | 262.82 | 224.46 | 164.76 | 106.43 | 55.68 | 33.68 | 17.59 | 13.597 | 7.04 |
| **50** | 436.15 | 365.42 | 300.76 | 207.16 | 116.13 | 38.78 | 10.38 | -7.8 | -6.003 | -9.46 |
| **60** | 635.85 | 528.02 | 425.06 | 283.56 | 145.83 | 29.88 | -10.92 | -35.01 | -28.203 | -29.16 |
| **70** | 905.55 | 750.62 | 597.36 | 393.96 | 195.53 | 28.98 | -30.22 | -64.04 | -53.003 | -52.06 |
| **80** | 1245.2 | 1033.2 | 817.66 | 538.3 | 265.2 | 36.08 | -47.52 | -94.89 | -80.403 | -78.16 |

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|---|---|---|---|---|---|---|---|---|---|---|
| | 5 | 2 | | 6 | 3 | | | | | |
| **90** | 1654.95 | 1375.82 | 1085.96 | 716.76 | 354.93 | 51.18 | -62.82 | -127.56 | -110.403 | -107.46 |
| **100** | 2134.65 | 1778.42 | 1402.26 | 929.16 | 464.63 | 74.28 | -76.12 | -162.05 | -143.003 | -139.96 |

**Table: 12a Case-2 LH Grade, Gray Matter, 500 Cells, Cisplatinum in Chemotherapy, Homogeneous Medium**

| **t** | **x=0.1** | **x=0.2** | **x=0.3** | **x=0.4** | **x=0.5** | **x=0.6** | **x=0.7** | **x=0.8** | **x=0.9** | **x=1** |
|---|---|---|---|---|---|---|---|---|---|---|
| **0** | 487.65 | 452.42 | 399.26 | 335.16 | 267.63 | 203.28 | 146.88 | 100.95 | 65.997 | 41.04 |
| **10** | 389.95 | 363.82 | 330.46 | 278.46 | 227.03 | 178.88 | 133.58 | 95.76 | 65.294 | 43.212 |
| **20** | 360.25 | 333.22 | 315.66 | 255.76 | 206.83 | 166.68 | 126.08 | 92.39 | 64.505 | 44.804 |
| **30** | 398.55 | 360.62 | 354.86 | 267.06 | 207.03 | 166.68 | 124.38 | 90.84 | 63.63 | 45.816 |
| **40** | 504.85 | 446.02 | 448.06 | 312.36 | 227.63 | 178.88 | 128.48 | 91.11 | 62.669 | 46.248 |
| **50** | 679.15 | 589.42 | 595.26 | 391.66 | 268.63 | 203.28 | 138.38 | 93.2 | 61.622 | 46.1 |
| **60** | 921.45 | 790.82 | 796.46 | 504.96 | 330.03 | 239.88 | 154.08 | 97.11 | 60.489 | 45.372 |
| **70** | 1231.75 | 1050.22 | 1051.66 | 652.26 | 411.83 | 288.68 | 175.58 | 102.84 | 59.27 | 44.064 |
| **80** | 1610.05 | 1367.62 | 1360.86 | 833.56 | 514.03 | 349.68 | 202.88 | 110.39 | 57.965 | 42.176 |
| **90** | 2056.35 | 1743.02 | 1724.06 | 1048.86 | 636.63 | 422.88 | 235.98 | 119.76 | 56.574 | 39.708 |
| **100** | 2570.65 | 2176.42 | 2141.26 | 1298.16 | 779.63 | 508.28 | 274.88 | 130.95 | 55.097 | 36.66 |

**Graphical Representation:** LH Grade: Low $\rho$, High $D$

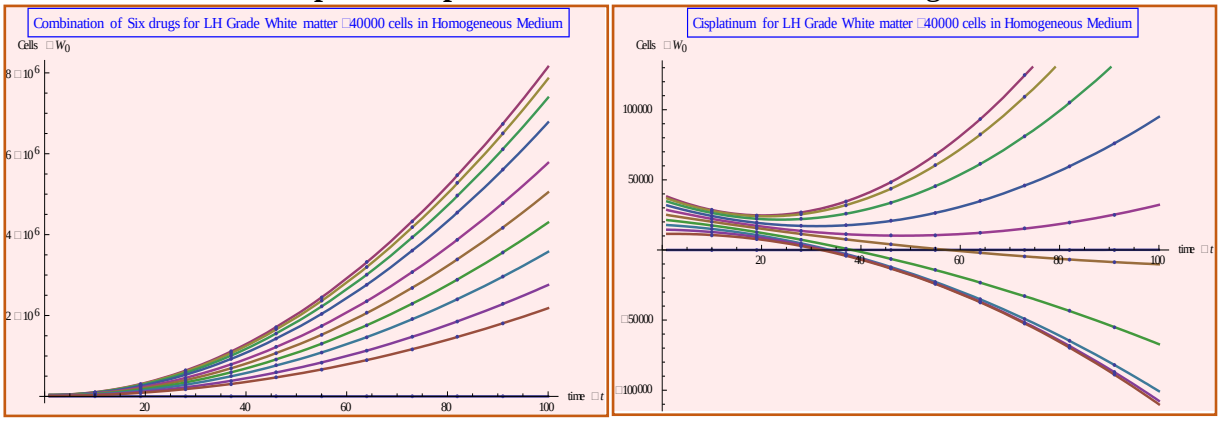

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**Fig. 13 & 13a: LH Grade, White Matter, 40000 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

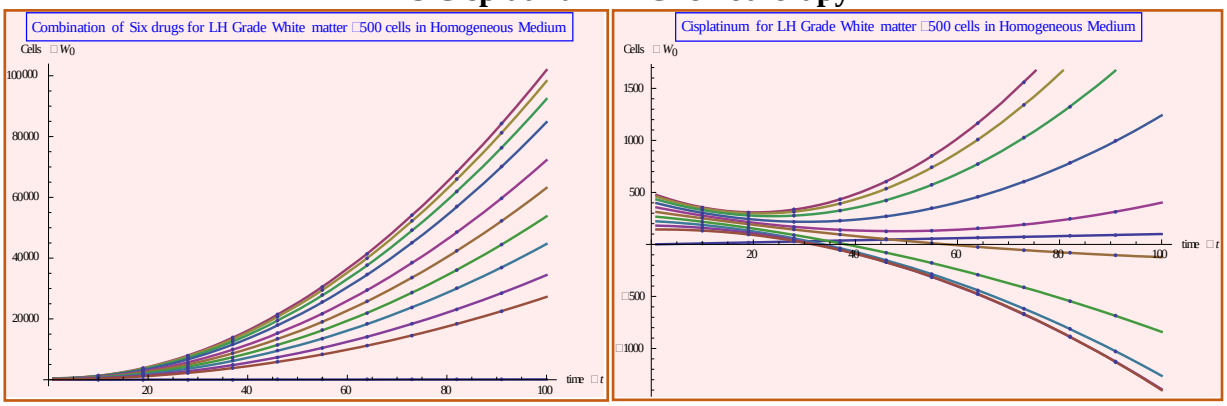


**Fig. 14 & 14a: LH Grade, White Matter, 500 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

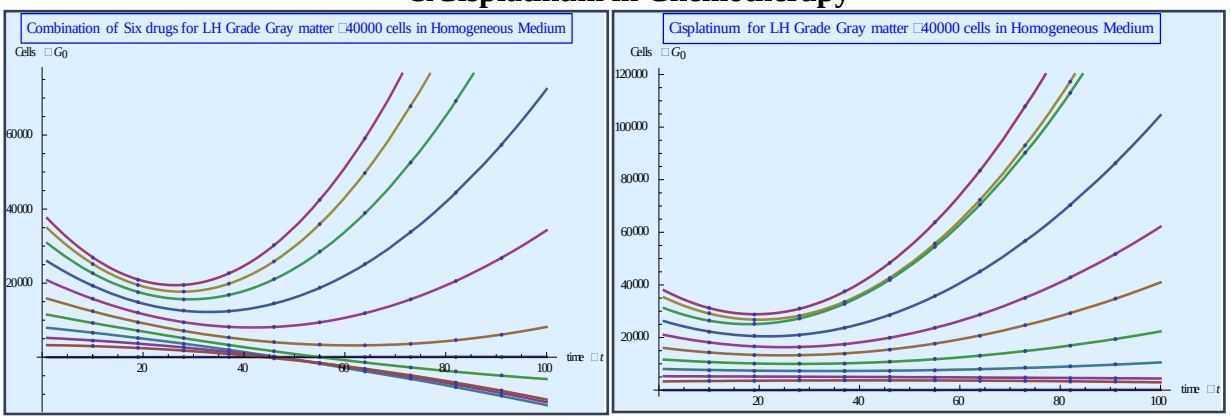


**Fig. 15 & 15a: LH Grade, Gray Matter, 40000 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

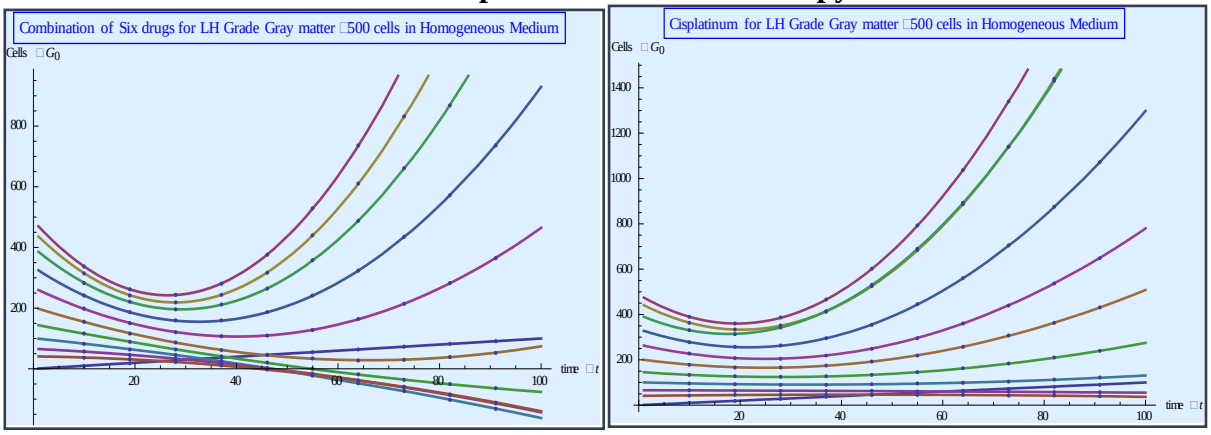


**Fig. 16 & 16a: LH Grade, Gray Matter, 500 cells, Combination of Six Drugs &Cisplatinum in Chemotherapy**

**Conclusion of case-2:** From the graph we can predict that after how many days second dose of drugs can be given to patient.

| | 40000 Cell | | 500 Cells | |
|---|---|---|---|---|
| **White Matter** | **Combination of Six Drugs** | **Cisplatinum** | **Combination of Six Drugs** | **Cisplatinum** |

| | | | | |
|---|---|---|---|---|
| **HH Grade** | After 20-22 days | After 30-32 days | After 20-22 days | After 30-32days |
| **HL Grade** | After 40-42 days | After 65-67 days | After 40-42 days | After 65-67days |
| **LH Grade** | After 10-12 days | After 20-22 days | After 10-12 days | After 20-22days |
| **Gray Matter** | **Combination of Six Drugs** | **Cisplatinum** | **Combination of Six Drugs** | **Cisplatinum** |
| **HH Grade** | After 25-27 days | After 40-42 days | After 28-30 days | After 40-42days |
| **HL Grade** | After 40-42 days | After 68-70 days | After 40-42days | After 68-70days |
| **LH Grade** | After 30-32 days | After 20-22 days | After 30-32 days | After 20-22days |

**Termination:**

We can conclude that the model taken into account is highly appropriate to estimate the effect of different drugs into chemotherapy treatment for the spatiotemporal behaviour of the tumor. After identifying the location, size, shape, diffusion and growth rate of specific tumor cells, this model can help to suggest the best type of therapy to maximize the survival time of the patient. Different drugs react differently and vary case to case. So, it is highly recommended to verify for every case.

Advantage of applying the new arrival - Kamal Transformation upon Variational Iteration method is used to reduce the tangible workload for finding the Lagrange Multiplier as well as save the time.

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