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AN APPROACH TO ESTIMATE THE PARAMETERS OF HOSSFELD, KORF AND LEVAKOVIC-III MODEL AND ITS APPLICATION ON TUMOUR GROWTH

UDOY NARAYAN GOGOI[1], PALLABI SAIKIA[2] and DIMPAL JYOTI MAHANTA[*]

[1,*]Assam Kaziranga University
Department of Mathematics
Jorhat, 785006, Assam, India
E-mail: nnsc.ung@gmail.com

[2]Nanda Nath Saikia College
Department of Mathematics
Titabar, 785630, Assam, India
E-mail: pallabisaikia.math@gmail.com

Abstract

Mathematical models are used to study the growth of tumour for more insight about the spread of the tumour in different parts of the body. In this paper three models, Hossfeld, Korf and Levakovic III are used and four different methods are introduced to estimate the models' parameters using standard growth data sets of tumour growth. The performances of the models have been analysed on the basis of a standard selection criterion. In this study it is found that the Hossfeld model performed well in comparison to the other two candidate models. The estimated parameters are logically and biologically significant.

1. Introduction

As the genetic materials of cells in the body of a host changes, solid tumours arise and responds differently to the growth regulations, which leads to uncontrolled growth of these cells [12]. As the tumour grows, these outer cells suck on the nutrients meant for the central cells and eventually the central cells become extensively deficient which cause them to die, and form a

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*Corresponding author; E-mail: dimpaljmahanta@gmail.com
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region of dead cells called the necrotic core. With time, the combined action of necrotic disintegration, accumulation of waste products [17], cell shedding [5] and mitotic inhibitory factors [7] reduces the rate of in vitro tumours. In vivo tumours keeps developing by releasing tumour angiogenesis factors stimulating the growth of new capillaries from adjacent vascular tissues into the tumour mass, restoring the nutrient supply deeper into the tumour making it grows further into a large mass [6]. Transcending from the size, malignant tumours become invasive and settles into other vascular cavities, forming secondary tumour growths. In spite of tremendous progress in all fields of science, technology and medicine, the cure to cancer has remained elusive.

Scientist and researchers are working tirelessly to elucidate the growth of tumour and its adversity and to explain the theoretical concepts practically, mathematical models come in practice [1]. Mathematical models are the intermediate interactive process that provides an insight about the spread or growth of the tumour in different parts of the body [2]. Thomlinson and Gray [16] proposed mathematical model that relates diffusion of nutrients with tumour heterogeneity. Tumour cells and normal cells are modelled as competing populations for space and other resources in an arbitrarily small volume of tissue within an organ. The mathematical models are used to predict phenotypic changes which are essential to examine invasive malignant behaviour [8]. They can give insights about the root cause of solid tumour growth, its invasion, metastasis and all the related phenomenon post-growth. Some mathematical models also help in understanding various treatment strategies and implementing them better in the forthcoming stages. 3-D architectural models help to study an underlining microcellular growth, which help to bring out maximum effect of treatment with minimum suffering of the patient [10]. Combined mathematical analysis of tumour growth helps to indicate correlation between clinical stage and tumour size and give proper instances of questions related to concepts like silent interval of tumour growth, probable avoidable and unavoidable diagnostic gap, apparent and actual survival time, 5 year cure rate, postsurgical period at risk, etc. [14].

In 1822 the Hossfeld model was proposed to study the tree growth [3]. Kiviste [9] found that Hossfeld model was one of the best models to study the volume growth of tumour. The mathematical form of the Hossfeld model is

$$y = \frac{t^c}{b + \frac{t^c}{a}}$$

The Hossfeld model became the best fit to individual data and also gave combination of optimum merit and has been conveniently suitable for extended modifications [3]. The Hossfeld model has been as accurate as the Chapman-Richard model, which pre-dominates the growth studies. In 1939 [9] proposed the Korf's Model and was published by Lundqvistin 1975. Stage [15] reviewed the Korf's model and used to study hight growth of the forests. Stage [15] used the Korf equation to study the plant growth. The Levakovic III (1935) model is basically a modification of the Hossfeld model. This model was published in Serbian over half a century ago. Kiviste [9] found that Levakovic III model is one of the most accurate models for growth study. The mathematical form of the Korf model is

$$y = ae^{-bt^{-c}}$$

The mathematical form of the Levakovic III model is

$$y = a\left(\frac{t^2}{b + t^2}\right)^c$$

where, y is the size of the tumour at the initial state, tis the time taken and a, b, c are parameters of the models.

2. Material and Method

In this paper an attempt has been made to introduce few methods of estimation for the candidate models based on the idea given by Borah and Mahanta [11]. The performances of the models have been analyzed by using the selection criterion given in a section below. This study involves the tumour growth in patients with quantitatively measurable neoplastic tumour. In this study nine data sets are used. The data set given in the table 1 are relating to tumour weights published by De Wys, 1972 [4]. The data of tumour measurement of eight male patients with bronchogenic carcinomas published by Schwartz [14] is given in table 2 to table 9 and are used to study in this paper. The required data sets are presented below in nine tabular forms.

Table 1. Comparison of tumour weights in double tumour group and Single tumour group.

Experiment days	Tumour weights
15	1.46
18	2.68
20	3.43
22	4.58
25	6.27

Table 2. Individual measurement for Pt. L.H.-RLL epidermoid care.

Time	Post.-ant.diam,cm
1 week	3
2 weeks	3.2
7 weeks	3.5
16 weeks	4.2
32 weeks	5.3
35 weeks	5.2
37 weeks	5.2
53 weeks	7.2

Table 3. Individual measurement for pt. M.B.-RUL anaplastic epidermoid care.

Time	Post.-ant.diam,cm
12 days	15.3
13 days	15.2
22 days	15.6
40 days	15.8
48 days	16.1
55 days	16.3
61 days	17.2
73 days	17.6
83 days	17.7

Table 4. Individual measurement for Pt. L.H.-RLL epidermoid care.

Time	Post.-ant.diam,cm
2 weeks	7.7
9 weeks	8.7
16 weeks	9.4
27 weeks	10.6
61 weeks	15.5
63 weeks	15.6

Table 5. Individual measurement for Pt. M.N.-LLL anaplastic epidermoid care.

Time	Post.-ant.diam,cm
1 day	2.3
17 days	2.6
36 days	2.7

70 days	2.9
72 days	2.9
79 days	3
85 days	3.2
102 days	3.4

Table 6. Individual measurement for Pt. J.S.,II-RLL anaplastic epidermoid care.

Time	Post.-ant. diam, cm
14 months	1.4
15 months	1.5
16.5 months	1.6
17 months	1.6
18 months	1.7
33.5 months	2.7
35.5 months	3.1
39.5 months	3.5

Table 7. Individual measurement for Pt. H.J.-LUL epidermoid care.

Time	Post.-ant.diam,cm
2 day	5.1
14 days	5.3
22 days	5.4
29 days	5.4
36 days	5.5
43 days	5.6
48 days	5.6
50 days	5.6

58 days	5.7
63 days	5.9

Table 8. Individual measurement for Pt. L.H.-RLL epidermoid care.

Time	Post.-ant.diam,cm
3 weeks	1.8
8.3 weeks	2.2
9 weeks	2.2
2.56 weeks	3.3
29.3 weeks	3.5
31.6 weeks	3.9
38 weeks	4.4
39.3 weeks	4.5
41 weeks	4.7
51.5 weeks	5.4
52.8 weeks	5.9
55 weeks	6.1
55.7 weeks	6.1
57 weeks	6.1
57.5 weeks	6.2
58 weeks	6.3
59.5 weeks	6.3
61 weeks	6.9
62 weeks	7.4
69 weeks	8.9
76 weeks	9.7

Table 9. Individual measurement for Pt. M.M..-RUL epidermoid care.

Time	Post.-ant.diam,cm
2 days	3.2
35 days	4.6
38 days	4.8
43 days	4.9
50 days	5
85 days	6.8
126 days	9.5
127 days	9.4
148 days	10.3
182 days	8.2
185 days	7.7
189 days	7.5

In the tables, RUL indicates right upper lobe, LUL indicates left lower lobe, LLL indicates left lower lode, RLL indicates right lower lobe, RML indicates right middle lobe. Pt. refers to Patient initiations.

3. Methods of Estimation

Most of the literature discussed in this study used to fit the candidate models by using some well-known algorithm. This study is trying to introduce some new methods of estimation by which one can easily fit the candidate models.

For Hossfeld Model

Method I

Let y_1, y_2 and y_3 be three integral forms of the Hossfeld model, such that

$$y_1 = \frac{t_1^c}{b + \frac{t_1^c}{a}} \tag{1}$$

$$y_2 = \frac{t_2^c}{b + \frac{t_2^c}{a}} \tag{2}$$

$$y_3 = \frac{t_3^c}{b + \frac{t_3^c}{a}} \tag{3}$$

Where, t_1, t_1 and t_1 are the time intervals of the observations.

From equation (1) we can have

$$b = \frac{at_1^c - y_1 t_1^c}{ay_1} \tag{4}$$

From equation (2) we can have

$$b = \frac{at_2^c - y_2 t_2^c}{ay_2} \tag{5}$$

From equation (3) we can have

$$b = \frac{at_3^c - y_3 t_3^c}{ay_3} \tag{6}$$

Solving equations (4) and (5) we have

$$a = \frac{y_1 y_2 (t_1^c - t_2^c)}{(y_2 t_1^c - y_1 t_2^c)} \tag{7}$$

Solving equations (5) and (6) we have

$$a = \frac{y_1 y_2 (t_1^c - t_2^c)}{(y_2 t_1^c - y_1 t_2^c)} \tag{8}$$

Assuming the parameter c as the known parameter we can estimate the parameter a either from equation (7) or from the equation (8). The parameter

b can be estimated from any one of the equations (4), (5) or (6) using estimated value of a and known value of c.

Method II

The Hossfeld model can be written as $y = \frac{at^c}{ab + t^c}$

Considering $B = ab$ and assuming c as known parameter we can have $y = \frac{a}{Bt^{-c} + 1}$

Consider $Y = \frac{1}{y} = \frac{Bt^{-c} + 1}{a}$

Now,

Let,

$$S_1 = \sum_{i=1}^{m} Y_i \tag{9}$$

$$S_1 = \frac{m + BS_1^c}{a}$$

Where, $S_1^c = \sum_{i=1}^{m} t_i^{-c} = \sum_{i=1}^{m} i^{-c}$

Also,

$$S_2 = \frac{m + BS_2^c}{a} \tag{10}$$

Where $S_2^c = \sum_{i=m+1}^{2m} (i)^{-c}$

From equation (9) we have

$$a = \frac{m + BS_1^c}{S_1} \tag{11}$$

From equation (10) we have

$$a = \frac{m + BS_2^c}{S_2} \tag{12}$$

Solving equations (11) and (12) we have

$$B = \frac{m(S_1 - S_2)}{S_2 S_1^c - S_1 S_2^c}$$

Using the value of B, we can estimate the parameter a and b as

$$a = \frac{m(S_2 S_1^c - S_1 S_2^c) + m(S_1 - S_2)}{S_1(S_2 S_1^c - S_1 S_2^c)}$$

$$b = \frac{B}{a}$$

Method III

Considering the value of the parameter c from Method I, the Hossfeld model can be written as $Y = BX + A$

Where, $Y = \frac{1}{y}$, $A = \frac{1}{a}$, $B = b$ and $X = t^{-c}$

The least square method is used to estimate the parameters a and b

Where $A = \frac{1}{n}\sum Y - \frac{\Sigma x}{n}$ and $B = \frac{n\sum XY - \sum X \sum Y}{n\sum X^2 - (\sum X)^2}$

Method IV

In this method we consider the parameter c as known parameter from the method II and the method of least square is used to estimate the parameters a and b.

For Korf Model

Method I

Let y_1, y_2 and y_3 be three integral forms of the Korf model, such that

$$y_1 = ae^{-bt_1^{-c}} \tag{13}$$

$$y_1 = ae^{-bt_1^{-c}} \tag{14}$$

$$y_1 = ae^{-bt_1^{-c}} \tag{15}$$

From equation (13) we have

$$b = t_1^c \log\left(\frac{y_1}{a}\right) \tag{16}$$

From equation (14) we have

$$b = t_2^c \log\left(\frac{y_2}{a}\right) \tag{17}$$

From equation (15) we have

$$b = t_2^c \log\left(\frac{y_2}{a}\right) \tag{18}$$

From equation (16) and (17) we have

$$a = e^{\frac{t_2^c \log y_2 - t_1^c \log y_1}{t_2^c - t_1^c}}$$

From equation (16) and (18) we have

$$a = e^{\frac{t_3^c \log y_3 - t_1^c \log y_1}{t_3^c - t_1^c}} \tag{19}$$

Assuming the parameter c as the known parameter we can estimate the parameter a from the equations (18) or (19). The parameter b can be estimated from the equations (16) or (17) by using the value of a.

Method II

Let us consider c to be known and $m = \frac{n}{2}$

The Korf model can be written as

$$\log y = \log a - bt^{-c}$$

Let, $Y = \log y = \log a - bt^{-c}$

Now,

$$S_1 = \sum_{i=1}^{m} Y_i$$

$$S_1 = m \log a - bS_1^c \tag{20}$$

Similarly,

$$S_2 = m \log a - bS_2^c \tag{21}$$

Where,

$$S_1^c = \sum_{i=1}^{m} t_i^{-c} = \sum_{i=1}^{m} i^{-c}$$

$$S_2^c = \sum_{i=m+1}^{2m} (i)^{-c}$$

From equations (20) and (21) we can estimate the parameter b as

$$b = \frac{S_2 - S_1}{S_1^c - S_1^c}$$

Using the estimated value of b we can estimate the parameter a from the equation (20) as

$$a = e^{\frac{S_2 S_1^c - S_1 S_2^c}{m(S_1^c - S_2^c)}}$$

Again, by using the values of the estimated parameters a and b we can estimate the parameter c as

$$c = \frac{\log b - \log\left(\log\left(\frac{a}{y}\right)\right)}{\log t}$$

Method III

Considering the value of the parameter c from Method I, the Korf model can be written as $Y = BX + A$

Where, $Y = \log y$, $B = b$, $X = t^{-c}$ and $A = \log a$

The least square method is used to estimate the parameters a and b

Where $A = \frac{1}{n}\sum Y - \frac{\sum X}{n}$ and $B = \frac{n\sum XY - \sum X \sum Y}{n\sum X^2 - (\sum X)^2}$

Method IV

In this method we consider the parameter c as known parameter from the method II and the method of least square is used to estimate the parameters a and b.

For Levakovic III model

Method I

Let y_1, y_2 and y_3 be three integral forms of the Levakovic III model, such that

$$y_1 = a\left(\frac{t_1^2}{b + t_1^2}\right)^c \tag{22}$$

$$y_2 = a\left(\frac{t_2^2}{b + t_2^2}\right)^c \tag{23}$$

$$y_3 = a\left(\frac{t_3^2}{b + t_3^2}\right)^c \tag{24}$$

From equations (22) and (23) we have

$$\log\left(\frac{y_1}{y_2}\right) = c \log\left(\frac{\frac{t_1^2}{b + t_1^2}}{\frac{t_2^2}{b + t_2^2}}\right) \tag{25}$$

From equations (23) and (24) we have

$$\log\left(\frac{y_2}{y_3}\right) = c\log\left(\frac{\frac{t_2^2}{b+t_2^2}}{\frac{t_3^2}{b+t_3^2}}\right) \tag{26}$$

Assuming b as the known parameter from equations (25) we can estimate the parameter c as

$$c = \frac{\log\left(\frac{y_1}{y_2}\right)}{\log\left(\frac{\frac{t_1^2}{b+t_1^2}}{\frac{t_2^2}{b+t_2^2}}\right)}$$

Using the estimated values of b and c we can estimate the parameter a as

$$a = \frac{y_1}{\left(\frac{t_1^2}{b+t_1^2}\right)^c}$$

Method II

Assuming the parameter c as known parameter and taking $m = \frac{n}{2}$ we proceed

The Levakovic III model can be written as

$$Y = \frac{bt^{-2}+1}{a^{\frac{1}{c}}} \tag{27}$$

Where, $Y = \frac{1}{y^{\frac{1}{c}}}$

Let,

$$S_1 = \sum_{i=1}^{m} Y_i$$

$$S_1 = \frac{m + bS_1^c}{a^{\frac{1}{c}}} \tag{28}$$

$$S_2 = \frac{m + bS_2^c}{a^{\frac{1}{c}}} \tag{29}$$

Where

$$S_1^c = \sum_{i=1}^{m} t_i^{-c} = \sum_{i=1}^{m} i^{-c}$$

$$S_2^c = \sum_{i=m+1}^{2m} (i)^{-c}$$

From equations (28) and (29) we can estimate the parameter b as

$$a = \frac{m(S_1 - S_2)}{S_2 S_1^c - S_1 S_2^{cv}}$$

Using the estimated value of the parameter b we can estimate the parameter a from equation (38) as

$$a = \left(\frac{m(S_1 - S_2)}{S_2 S_1^c - S_1 S_2^c} \right)^c$$

Method III

Considering the value of the parameter c from Method I, the Levakovic III model can be written as $Y = BX + A$

Where, $A = \frac{1}{a^{\frac{1}{c}}}$, $B = \frac{b}{a^{\frac{1}{c}}}$ and $X = \frac{1}{t^2}$

The least square method is used to estimate the parameters a and b

Where $A = \frac{1}{n} \sum Y - \frac{\sum X}{n}$ and $B = \frac{n \sum XY - \sum X \sum Y}{n \sum X^2 - (\sum X)^2}$

Method IV

In this method we consider the parameter c as known parameter from the method II and the method of least square is used to estimate the parameters a and b.

4. Selection Criteria for Best fit Model

After fitting the growth models using different methods of estimation, the best fit model is selected based on the standard selection criteria adopted from the paper [17] involving four distinct steps.

5. Results and Discussion

The results of the methods applied in the three models taken for study the growth of tumour using the standard data sets are given below. In the first step we take into account only those methods for each data set which survive with the least RMSE (Root Mean Square Error) values and the maximum R_a^2 (Adjusted R square value). The rest are rejected. The selected one are further studied for R^2 and $R^2_{\text{prediction}}$ values which gives us the best fit results. The R^2 values shows that how well the data points fit in the growth model and the $R^2_{\text{prediction}}$ indicates the predictive capacity of the model. The most efficient method and model in this study is finally selected on the basis of the optimum value of each of these criteria.

The results for each data set of the four methods of each model with parameters a, b, care shown in the Table 10 to Table 18.

Table 10. Results of the different methods corresponding to data set of Table 1.

Growth model	methods	a	b	c	RMSE	R_a^2	R^2 (in %)	$R^2_{prediction}$ (in %)
Hossfeld	I	-60.059	0.7016	0.8479	0.2717	0.9453	97.2683	95.1539
	II	-0.8888	1.7686	0.2000	0.1401	0.9855	99.2732	98.9386
	III	660.578	0.6842	0.8479	0.2977	0.9344	96.7195	90.1420

	IV	-0.8259	1.8723	0.2000	0.3036	0.9318	96.5888	90.4980
Korf	I	5.8989	0.7162	0.8236	1.1423	0.0342	51.7087	12.1472
	II	4.1674	1.2880	0.8284	1.0867	1.3059	115.293	99.9109
	III	8.2993	1.8111	0.8236	0.5865	0.7453	87.2664	69.3903
	IV	8.2506	1.8054	0.8284	0.5883	0.7438	87.1903	63.1763
Levakovic III		7.4734	-118.59	0.1955	1.0828	0.9393	94.9427	99.9097
	II	5.1811	-0.9717	-0.365	0.9298	0.7495	87.4754	99.8514
	III	1.8603	-10.443	0.1955	2.1362	-1.752	-37.574	-329.028
	II	5.1811	-0.9717	-0.365	0.9298	0.7495	87.4754	99.8514

Table 11. Results of the different methods corresponding to data set of Table 2.

Growth model	methods	a	b	c	RMSE	R_a^2	R^2 (in %)	$R^2_{prediction}$ (in %)
Hossfeld	I	2.4787	-0.070	-0.6188	0.3929	0.8752	91.088	85.5274
	II	2.2963	-0.086	-0.590	0.3910	0.8764	91.174	86.109
	III	2.4008	-0.074	-0.619	0.3874	0.8787	91.337	86.111
	IV	2.3588	-0.081	-0.590	0.3883	0.8778	91.273	85.900
Korf	I	9.6322	0.8573	0.2455	1.0671	0.0798	34.271	12.2363
	II	506881	1.7836	0.9733	1.3603	104177	129.84	99.9485
	III	19.134	2.0016	0.2455	0.6307	0.6786	77.041	58.7542
	IV	5.8860	0.8249	0.9733	0.8384	0.4320	59.431	28.075
Levakovic III	I	17.919	-349415	0.1214	0.9009	0.3442	53.155	9.16875
	II	5.6895	0.6067	1.3497	1.0887	0.0429	31.585	5.3914

	III	4.3155	20.4438	0.1214	1.2944	-0.3539	3.2861	-84.946
	IV	4.8668	0.5098	1.3497	1.0324	0.1388	38.485	-11.010

Table 12. Results of the different methods corresponding to data set of Table 3.

Growth model	methods	a	b	c	RMSE	R_a^2	R^2 (in %)	$R_{prediction}^2$ (in %)
Hossfeld	I	15.2467	-0.0002	-1.6652	0.2302	0.9147	93.600	90.36823
	II	14.9749	-0.0006	-1.3000	0.1718	0.9525	96.434	94.96733
	III	15.1610	-0.0003	-1.6652	0.173	0.9521	96.405	94.40274
	IV	14.9745	-0.0006	-1.3000	0.708	0.9530	96.474	95.04084
Korf	I	15.8000	31.0973	10.210	5.1995	-42.55	-3166.4	-3276.971
	II	15.0010	-0.0081	-1.4493	0.2613	0.8900	91.750	86.8163
	III	16.4140	0.0703	10.209	0.8367	-0.1278	15.413	-24.139
	IV	15.260	-0.0072	-1.4493	0.1662	0.9554	96.659	95.2316
Levakovic III	I	16.1448	-57.3951	0.0113	0.8535	-0.1699	12.250	-49.9777
	II	16.7869	0.0623	1.5335	0.7878	-0.0001	24.996	1.7867
	III	15.6451	8.3644	0.0113	1.1333	-1.0693	-55.200	-163.0560
	IV	16.5588	0.0675	1.5335	0.7564	0.0784	30.879	-1.5202

Table 13. Results of the different methods corresponding to data set of Table 4.

Growth model	methods	a	b	c	RMSE	R_a^2	R^2 (in %)	$R_{prediction}^2$ (in %)
Hossfeld	I	7.1202	-0.0106	-1.0647	1.4187	0.6642	79.853	59.9430
	II	5.7833	-0.0377	-0.600	0.9564	0.8474	90.843	83.5980
	III	7.0142	-0.0122	-1.0647	1.002	0.8326	89.954	79.8035
	IV	5.871	-0.036	-0.600	0.982	0.8391	90.345	82.7404
Korf	I	9.4014	5.0090	6.5045	4.7514	-2.7667	-126.0	-296.668
	II	5.6161	-0.2463	-0.7939	0.9845	0.8382	90.296	83.5286

	III	11.614	0.4142	6.5405	2.7416	-0.2541	24.756	-47.9931
	IV	5.6871	-0.2436	-0.7939	0.9845	0.8382	90.296	83.6074
Levakovic III	I	34.566	-7941210.3	0.0908	2.9376	-0.4398	13.607	-97.9363
	II	14.349	0.650	1.242	2.5402	-0.0767	35.402	10.0115
	III	10.44	-46.740	0.0908	2.3104	-0.1093	46.559	-18.0580
	IV	12.185	0.5049	1.2428	2.4088	0.0319	4.0914	-18.8142

Table 14. Results of the different methods corresponding to data set of Table 5.

Growth model	methods	a	b	c	RMSE	R_a^2	R^2 (in %)	$R_{prediction}^2$ (in %)
Hossfeld	I	-0.584	2.1460	0.0309	0.0743	0.9259	94.71	92.17179
	II	2.3320	-0.0200	-0.900	0.0734	0.9277	94.833	93.9763
	III	-0.613	2.0637	0.0309	0.0693	0.9356	95402	92.1017
	IV	2.2858	-0.0223	-0.9000	0.0719	0.9307	95.051	94.2505
Korf	I	2.9001	4.3131	6.1147	0.8301	-8.2424	-560.20	-608.78
	II	2.3033	-0.0563	-0.9298	0.0729	0.9289	94.921	93.8244
	III	2.9487	0.2503	6.1147	0.2371	0.2456	46.119	11.6533
	IV	2.2644	-0.0579	-0.9298	0.0669	0.9399	95.712	94.9377
Levakovic III	I	2.9029	-20.077	0.0663	0.1486	1.0250	101.79	97.16119
	II	3.1182	0.1172	2.7456	0.2055	0.4337	59.551	43.1502
	III	2.8663	-38.8373	0.0663	0.1094	1.8366	159.76	225.4827
	IV	3.0246	0.1149	2.7456	0.1915	0.5080	64.857	39.9323

Table 15. Results of the different methods corresponding to data set of Table 6.

Growth model	methods	a	b	c	RMSE	R_a^2	R^2 (in %)	$R_{prediction}^2$ (in %)
Hossfeld	I	1.3913	-0.005	-2.1923	0.3189	0.7636	83.116	73.3265
	II	1.2730	-0.0415	-1.200	0.2096	0.898	92.705	89.3083

	III	1.4308	-0.0048	-2.1923	0.324	0.755	82.541	67.6365
	IV	1.2738	-0.0414	-1.200	0.2101	0.8974	92.673	89.2580
Korf	I	1.600	7.4873	6.1147	1.0632	-1.627	-87.65	-218.37
	II	2.656	2.216	1.002	0.7922	1.1333	109.52	94.3409
	III	2.1217	0.4211	6.114	0.7316	-0.2442	11.122	-53.942
	IV	2.655	0.819	1.002	0.948	0.1775	41.253	-0.2284
Levakovic III	I	2.9019	-1958081.7	0.0482	0.8856	-0.823	-30.21	-145.730
	II	2.6466	0.687	1.216	0.6858	-0.931	21.915	-9.724
	III	1.6622	-45.722	0.0482	0.8109	-0.4918	-6.559	-103.95
	IV	2.153	0.510	1.216	0.6939	-0.1193	20.048	-43.569

Table 16. Results of the different methods corresponding to data set of Table 7.

Growth model	methods	a	b	c	RMSE	R_a^2	R^2 (in %)	$R_{prediction}^2$ (in %)
Hossfeld	I	4.6733	-0.0179	-0.3640	0.0555	0.9117	93.133	89.89950
	II	4.9843	-0.0071	-0.6000	0.0546	0.9147	93.366	90.39359
	III	4.7179	-0.0169	-0.3640	0.0541	0.9161	93.473	90.0144
	IV	4.9665	-0.0073	-0.6000	0.0541	0.9162	93.484	90.69635
Korf	I	1.6000	7.4873	6.1147	1.0632	-1.6271	-87.65	-218.3742
	II	5.2049	-0.0058	-1.3346	0.0711	0.8553	88.746	85.77384
	III	5.5542	0.0860	6.1147	0.1608	0.2595	42.409	16.02971
	IV	5.2013	-0.0055	-1.3346	0.0664	0.8737	90.174	88.16203
Levakovic III	I	6.2221	-5211.3	0.0234	0.075	0.8392	87.7494	78.3528
	II	5.6787	0.0601	1.8425	0.1552	0.3101	46.339	33.1627
	III	5.7118	-141.5	0.0234	0.0499	0.9288	94.461	92.0965
	IV	5.5944	0.0575	1.8425	0.1351	0.4776	59.376	38.8281

Table 17. Results of the different methods corresponding to data set of Table 8.

Growth model	methods	a	b	c	RMSE	R_a^2	R^2 (in %)	$R^2_{prediction}$ (in %)
Hossfeld	I	-9.684	0.6588	0.3587	0.5324	0.9242	93.181	91.77516
	II	-0.921	1.6267	0.100	0.470	0.9408	94.677	93.76296
	III	-8.606	0.7140	0.3587	0.5083	0.9309	93.783	92.2077
	IV	9.4315	0.5338	0.8000	0.9677	0.750	77.471	71.16482
Korf	I	6.3986	0.7885	0.8736	1.5197	0.3827	44.440	35.3977
	II	2.4572	-0.0483	-1.1174	0.7813	0.8368	85.311	82.8158
	III	7.0697	1.7962	0.8736	1.1713	0.6333	66.995	59.14183
	IV	2.4324	-0.0468	-1.1174	0.6772	0.8774	88.966	87.62075
Levakovic III	I	8.5082	-1869.3	0.236	0.5641	0.9150	92.353	90.57969
	II	6.7394	2.8022	0.9885	1.6704	0.2541	32.874	26.4468
	III	4.391	45.6071	0.2360	2.1756	-0.2752	-13.87	-41.5591
	IV	5.1173	2.2390	0.9885	1.7263	0.2033	28.304	11.31055

Table 18. Results of the different methods corresponding to data set of Table 9.

Growth model	methods	a	b	c	RMSE	R_a^2	R^2 (in %)	$R^2_{prediction}$ (in %)
Hossfeld	I	14.5011	0.2435	0.6347	1.2766	0.5664	63.8647	56.6843
	II	10.434	0.3516	1.3000	1.3383	0.5233	60.2828	51.21669
	III	14.6364	0.2509	0.6347	1.2876	0.559	63.2342	55.9831
	IV	8.0124	0.2054	1.3000	1.4109	0.4703	55.8564	48.76815
Korf	I	8.3030	1.0488	0.8725	1.4711	0.4241	52.0076	43.73704
	II	11.4042	1.9892	0.6268	1.6773	0.2513	37.6116	27.62832
	III	9.0759	1.1767	0.8725	1.3263	0.5319	60.9907	54.98856
	IV	10.8052	1.3273	0.6268	1.281	0.5634	63.6192	57.3389

Levakovic III	I	7.0612	-40.19	0.1890	0.894	0.8836	90.2965	93.8489
	II	8.7291	1.1418	1.3176	1.7686	0.168	30.6379	23.48437
	III	9.6519	-912.7	0.1890	1.3847	0.4898	57.482	48.3476
	IV	7.1749	0.9321	1.3176	1.6089	0.3112	42.5982	33.5889

In each of the data set above we can see that some of the methods produce results that are out rightly logically insignificant and shows inconsistency. We reject such methods straightaway.

From the methods that survive the first analysis, we check the method with the lowest RMSE values. After checking the values of RMSE we check the values of R_a^2 for the methods. The higher the value of R_a^2 and approaches to 0.99 the performance of the method is better.

In the final level of checking, we analysis the R^2 and $R^2_{\text{prediction}}$ values of the surviving methods. A high value of R^2 shows us that the data set points fit well and the high value of $R^2_{\text{prediction}}$ gives us the model that has higher predictive capacity.

The best fit results obtained satisfying all these criteria in our study are detailed in the table below.

The survive methods having the lowest RMSE for each table are given in Table 19.

Table 19. List of surviving methods having the lowest RMSE corresponding to nine data sets used.

Sets of data in the Table	Model	Method	RMSE	R_a^2	R^2 (in %)	$R^2_{prediction}$ (in %)
Table 1	Hossfeld	II	0.14013	0.98546	99.27324	98.93858
Table 2	Hossfeld	III	0.38741	0.87872	91.33702	86.11175
Table 3	Korf	IV	0.16629	0.95545	96.65911	95.23169
Table 4	Hossfeld	II	0.95640	0.84738	90.84299	83.59809
Table 5	Korf	IV	0.06690	0.93997	95.71229	94.93775
Table 6	Hossfeld	II	0.20962	0.89788	92.70537	89.30834

Table 7	Levakovic III	III	0.04987	0.92879	94.46122	92.09652
Table 8	Hossfeld	II	0.47038	0.94085	94.67678	93.76296
Table 9	Levakovic III	I	0.89366	0.88356	90.29651	93.84898

In our study from the above analysis, we have observed that the method II of the Hossfeld model gives efficient results for four different data sets. Similarly, method IV of the Korf model gives efficient results for two different data sets. All other methods give efficient results only once and hence rejected the efficiency of these methods. In this study methods producing R_a^2 value less than 0.99 or $R_{\text{prediction}}^2$ value less than 0.90 are rejected due to undermining efficiency level.

The final finding of the best fit methods of this study with the analysis based on the prescribed criteria are shown below:

Table 20. The final list of best fit methods and models.

Sets of data in the Table	Model	Method	RMSE	R_a^2	R^2 (in %)	$R_{prediction}^2$ (in %)
Table 1	Hossfeld	II	0.14013	0.98546	99.27324	98.93858
Table 3	Korf	IV	0.16629	0.95545	96.65911	95.23169
Table 5	Korf	IV	0.06690	0.93997	95.71229	94.93775

In this study we have observed that the Hossfeld Model with method II produced the highest predictive probability with the highest $R_{\text{prediction}}^2$ and R^2 values. It has also the highest R_a^2 value making it suitable method of the model in this study. On the other hand, the method IV of the Korf model has produced the least RMSE values among all the three models. Considering all these observations we can conclude that the method II of the Hossfeld model is the best fit method. This method is the most efficient method having high predictive capacity which is useful for further studies.

6. Conclusion

Analyzing the best fit model helps us in the prediction of the probable growth of tumour since its initiation helps to study required steps to be taken accordingly against the growth. It also helps us to study any further growth that may occur even after the regression of the primary growth. Tumour growth is a highly unpredictable and fatal phenomenon that is seen to be on rise. This study helps to decide on the model that best fit any data and gives a view of the future scope of analysis. Study about the tumour growth helps us to know more about the probabilities and reasons of occurrence of tumour which is necessary to understand the various actions related to the process of advancement of tumour in different individuals.

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