

**Original Research**

## **Mathematical Analysis of Birth Rate of Cancer Model**

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### **ABSTRACT:**

A model comprising four nonlinear differential equations describes the untreated spread of cancer from a primary to a secondary site. It takes into consideration the competition possibly delayed between healthy and malignant cells for resources at both sites. Within a proportionate range, different normal cell birth rates are taken into consideration. In this study, the equilibrium points of the model are computed numerically, and their stability was evaluated. By simulating cell behavior over time, the Runge-Kutta approach examines how changes in the birth rate affect the model. In our model. The study examined the effects of changing the birth rate on cell dynamics by comparing results from graphs with equilibrium points. To do the calculations, MATLAB 2014a was utilized.

**KEYWORDS:** Cancer Model, Birth Rate, Runge-Kutta, Mathematical Analysis.



## INTRODUCTION

The birth rate ( $\alpha_1$ ) is a key parameter in mathematical models explaining cell development and proliferation that is necessary to comprehend the dynamics of the system.

The pace at which healthy cells divide to generate new ones is known as the birth rate, and it plays a crucial role in maintaining tissue homeostasis and overall health.

Numerous biological and environmental factors, including as nutrition availability, chemical signaling, and interactions with neighboring cells, affect birth rates (Pinho, (2002)), (Alam, (2023)).

Understanding the dynamics of normal cell ( $x_1$ ) growth in relation to the birth rate ( $\alpha_1$ ) is essential for comprehending the genesis of malignant tumors.

Cancer cells may spread as a result of variations in the birth rates of healthy and malignant cells. The present study can examine how birth rates impact the stability of the biological system and pinpoint the circumstances that result in unchecked proliferation by integrating birth rates into mathematical models.

This study aims to provide new insights into how birth rates ( $\alpha_1$ ) influence normal cell growth and the spread of cancer cells (Turyn, (2014)).

The purpose of this study is to provide light on the relationship between birth rates ( $\alpha$ ) and cancer cell dissemination as well as normal cell proliferation.

The format of the paper is as follows: the study provides a model as a special case of no treatment for cancer spread in the following section.

The stability of the equilibrium point is examined in this section. There are several numerical examples in the next section. Next,

numerical simulation is covered in Section.

The final section contains the closing thoughts. The code for the model is in the last part (Abdulrashid, 2020; Xenophontos, 1998).

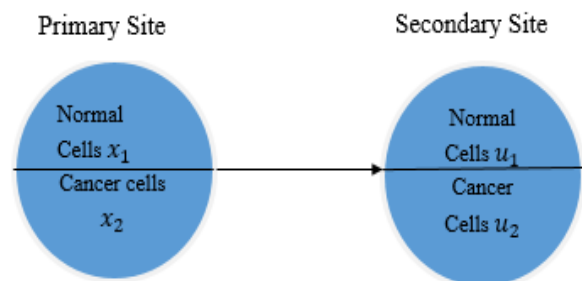
## The Model

The study employed logistic growth at both sites, where normal and cancerous cells competed with one another.

The length of ( $\tau$ ) between the time those cells leave the primary site and start interacting at the secondary site may be delayed in the second phase of the cancer cell cycle (Al-Johani, (2019)).

## Types of Cells and Their Locations:

1. **Primary Site:** contains the normal cells  $x_1(t)$ , and the cancer cells  $x_2(t)$ .
2. **Secondary Site:** contains the normal cells  $u_1(t)$ , and the cancer cells  $u_2(t)$ .



**Fig.1:** The Interaction between Normal Cells and Cancer Cells at the Primary and Secondary Site.

The interaction between normal and cancer cells in both the primary and secondary sites is described by the following differential equations (Mukherjee, (2010)):

**Primary Site Equations**

**1. Normal Cells ( $x_1$ ):**

$$\begin{aligned} & \frac{dx_1(t)}{dt} \\ = & \alpha_1 x_1(t) \left(1 - \frac{x_1(t)}{K_1}\right) \\ & - q_1 x_1(t) x_2(t), \end{aligned} \tag{1}$$

**Description:** This equation represents the growth of normal cells ( $x_1$ ), which is limited by the carrying capacity ( $K_1$ ), and reduced due to interactions with cancer cells ( $x_2$ ).

**2. Cancer Cells ( $x_2$ ):**

$$\begin{aligned} & \frac{dx_2(t)}{dt} \\ = & \alpha_2 x_2(t) \left(1 - \frac{x_2(t)}{K_2}\right) \\ & - q_2 x_1(t) x_2(t) \\ & - \delta x_2(t), \end{aligned} \tag{2}$$

**Description:** The growth of cancer cells ( $x_2$ ) is described by this equation. It is restricted by the carrying capacity ( $K_2$ ), impacted by interactions with normal cells ( $x_1$ ), and diminished as a result of migration away from the initial site.

**Secondary Site Equations**

**3. Normal Cells  $u_1(t)$ :**

$$\begin{aligned} & \frac{du_1(t)}{dt} \\ = & \beta_1 u_1(t) \left(1 - \frac{u_1(t)}{L_1}\right) \\ & - r_1 u_1(t) u_2(t), \end{aligned} \tag{3}$$

**Description:** This equation shows how the proliferation of normal cells ( $u_1$ ) at the

secondary site is hampered by the presence of cancer cells ( $u_2$ ) and restricted by the carrying capacity ( $L_1$ ).

**4. Cancer Cells  $u_2(t)$ :**

$$\begin{aligned} \frac{du_2(t)}{dt} = & \beta_2 u_2(t) \left(1 - \frac{u_2(t)}{L_2}\right) \\ & - r_2 u_1(t) u_2(t) \\ & + \varepsilon \delta x_2(t - \tau) \end{aligned} \tag{4}$$

**Description:** This equation describes the growth of cancer cells ( $u_2$ ) at the secondary site, their interaction with normal cells ( $u_1$ ), and the addition of cancer cells ( $x_2$ ) migrating from the primary site with a delay ( $\tau$ ).

**Parameters**

*Primary Site Parameters*

$\alpha_1$ : Birth rate of normal cells  $x_1$ , ( $0 < \alpha_1 < \alpha_2$ ).

$K_1$ : Carrying capacity for normal cells  $x_1$ , ( $0 < x_1 \leq K_1 \leq K_2$ ).

$q_1$ : Effect of cancer cells  $x_2$  on normal cells  $x_1$ ,  $0 < q_1 < \alpha_1$ .

$\alpha_2$ : Birth rate of cancer cells  $x_2$ , ( $0 < \alpha_1 < \alpha_2$ ).

$K_2$ : Carrying capacity for cancer cells  $x_2$ , ( $0 < K_1 \leq K_2$ ) and ( $0 < x_2 \leq K_2$ ).

$q_2$ : Effect of normal cells  $x_1$  on cancer cells  $x_2$ ,  $0 < q_2 < \alpha_2$ .

$\delta$ : is the rate at which cancer leaves the primary site ( $0 < \delta < \alpha_2$ ).

**Secondary Site Parameters:**

$\beta_1$ : Birth rate of the normal cells  $u_1$ , ( $0 < \beta_1 < \beta_2$ ).

$L_1$ : Carrying capacity for normal cells  $u_1$ , ( $0 < u_1 \leq L_1 \leq L_2$ ).

$r_1$  : Effect of cancer cells  $u_2$  on normal cells  $u_1$ ,  $0 < r_1 < \beta_1$  .

$\beta_2$ : Birth rate of cancer cells  $u_2$ , ( $0 < \beta_1 < \beta_2$ ).

$L_2$ : Carrying capacity for the cancer cells  $u_2$ , ( $0 < L_1 \leq L_2$ ) and ( $0 < u_2 \leq L_2$ ).

$r_2$ : Effect of normal cells  $u_1$  on cancer cells  $u_2$ ,  $0 < r_2 < \beta_2$  .

$\varepsilon$ : Proportion of cancer cells that migrate to the secondary site after leaving the primary site, ( $0 < \varepsilon \ll 1$ ).

$\tau$ : Time delay of cancer cell migration from the primary to the secondary site,  $0 \leq \tau$ , and  $-\tau \leq t$ .

**Initial conditions:**

- $x_1(0) > 0$ .
- $x_2(0) > 0$ .
- $u_1(0) > 0$ .
- $u_2(0) \geq 0$ .

**EQUILIBRIUM POINTS**

A point  $E = (x_1, x_2, u_1, u_2)$  is called a generic equilibrium point of the system, we discuss the stability of one state:

**1) The nonnormal equilibrium point:**

$$E = \left( 0, \frac{K_2(\alpha_2 - \delta)}{\alpha_2}, 0, \frac{L_2}{2} + \sqrt{\frac{L_2^2}{4} + \frac{\varepsilon \delta L_2 K_2 (\alpha_2 - \delta)}{\beta_2 \alpha_2}} \right),$$

Represents the case where the cancer has completely taken over both sites (no normal cells in both sites).

This equilibrium point is biologically relevant only if:  $\alpha_2 > \delta$ , and it is stable only if:

$$2\beta_1 < r_1 L_2 \left[ \left( 1 + \sqrt{1 + \frac{4\varepsilon \delta K_2 (\alpha_2 - \delta)}{L_2 \beta_2 \alpha_2}} \right) \right], \text{ and}$$

$$\alpha_1 \alpha_2 < q_1 K_2 (\alpha_2 - \delta)$$

**1. An Illustration of a Numerical Equation**

Determine whether or whether the steady points in Models (1) through (4) are stable. Considering the subsequent parameters:

$$\alpha_2 = 10, K_1 = 1460,$$

$$K_2 = 2100, q_1 = 0.0075, q_2 = 0.005, \delta = 0.1, \beta_1 = 2, \beta_2 = 12, L_1 = 1750, L_2 = 2300,$$

$$r_1 = 0.002, r_2 = 0.001, \tau = 0, \varepsilon = 0.0001.$$

In this section, we provide two sets of numerical examples to validate the two different solution cases.

**2) The first case is when  $\alpha_1 = 0.1$ , with the previous parameters:**

The equilibrium point  $(0, \tilde{x}_2, 0, \tilde{u}_2) = (0, 2079, 0, 2300)$ , and this equilibrium point is stable.

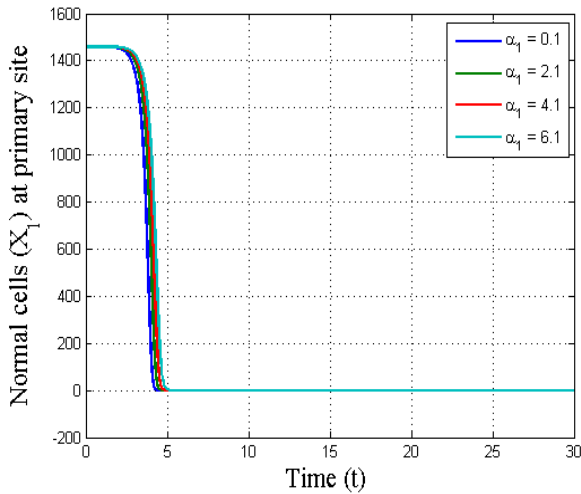
**3) The second case when  $\alpha_1 = 6.1$ , with the previous parameters:**

The equilibrium point  $(0, \tilde{x}_2, 0, \tilde{u}_2) = (0, 2079, 0, 2300)$ , and this equilibrium point is stable.

**NUMERICAL SIMULATION**

Comparison on the model (1)-(4) for  $0 \leq t \leq 30$ , with the pre-imposed parameters and the initial conditions:

$$x_1(0) = K_1, x_2(0) = 0.01, u_1(0) = L_1, \\ u_2(0) = 0.$$

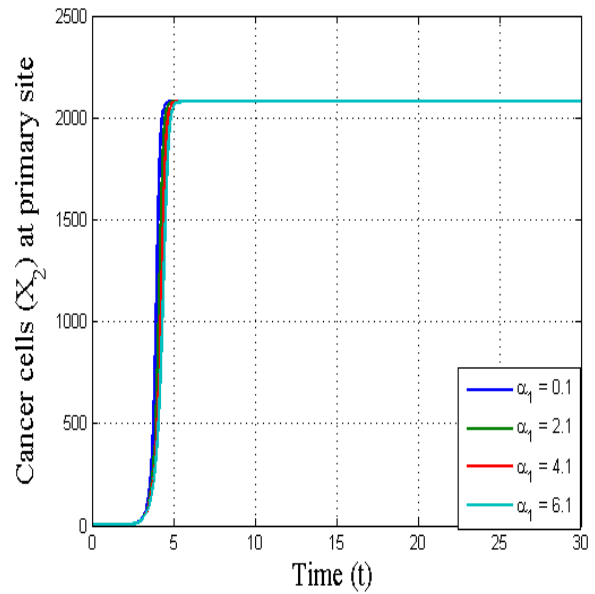


**Fig.1:** Variations in the concentration of the normal cells ( $x_1$ ) at the primary site with  $\alpha_1 = 0.1, 2.1, 4.1, 6.1$

In Fig.1, the effort showed that the concentration of normal cells ( $x_1$ ) in the primary site starts at 1460, after that the curve begins to decline rapidly at ( $t = 2$ ), and then after ( $t = 6$ ), the normal cells of the primary site are at a value close to zero.

As a result, normal cells ( $x_1$ ) drop in competition at the primary site.

Here the study found that there was a small effect of  $\alpha_1$  that does not affect the behaviour of the curve, and this effect is that smaller values of  $\alpha_1$  associated with the faster death of the normal cells ( $x_1$ ).



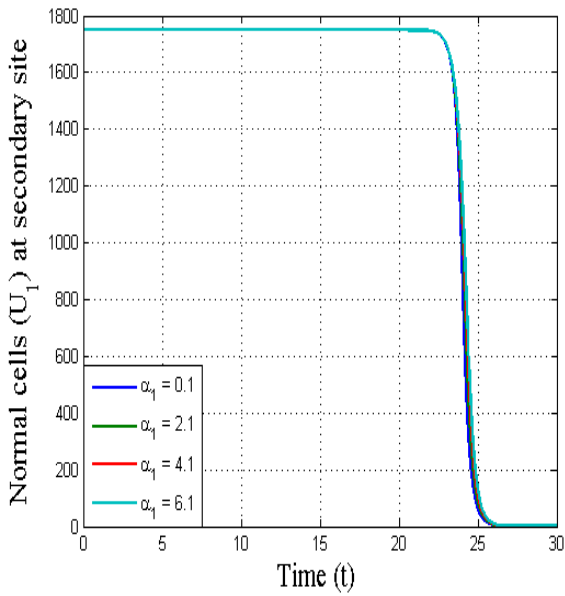
**Fig.2:** Variations in the concentration of the cancer cells ( $x_2$ ) at the primary site with  $\alpha_1 = 0.1, 2.1, 4.1, 6.1$

The effort noticed in Fig.2, that the cancer cells at the primary site ( $x_2$ ) start with a value of 0.01, then after ( $t = 2$ ) this number increases quickly, and when:

$\alpha_1 = 0.1, t = 5$ , the cancer cells  $x_2$  at the primary site stabilize at 2079 to the end of the period.

$\alpha_1 = 1.9, t = 6$ , the cancer cells  $x_2$  at the primary site stabilize at 2079 to the end of the period.

The study explained that smaller values of birth rate ( $\alpha_1$ ) are associated with faster growth of cancer cells ( $x_2$ ) at the primary site, which means that there is a time difference in stability between each curve and another.

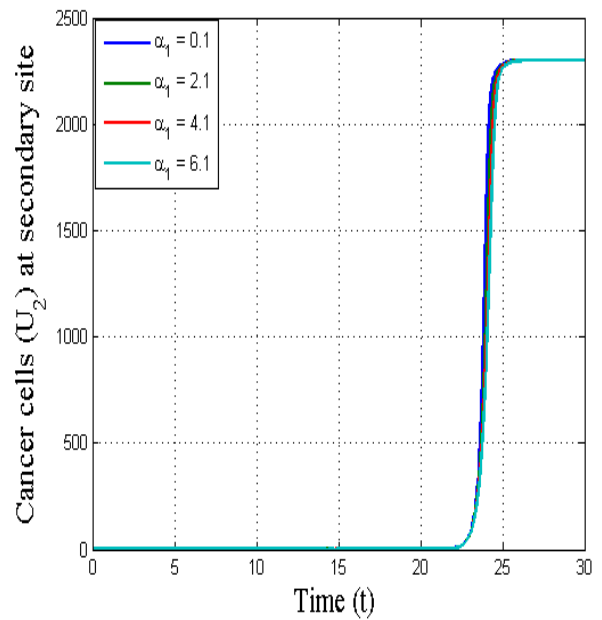


**Fig.3:** Variations in the concentration of the normal cells ( $u_1$ ) at the secondary site with  $\alpha_1 = 0.1, 2.1, 4.1, 6.1$

In Fig.3, the mathematical effort implied that the concentration of normal cells  $u_1$  at the secondary site starts at 1750, and it is constant at this value until  $t = 20$ .

After that, the curve begins to decline rapidly, and at ( $t = 30$ ) the normal cell ( $u_1$ ) is stable at zero.

Here the study noticed that smaller values of  $\alpha_1$  associated with the faster growth of the cancer cells ( $u_2$ ) and this effect is very simple and does not affect the behaviour of the curve.



**Fig.4 :** Variations in the concentration of cancer cells ( $u_2$ ) at the secondary site with  $\alpha_1 = 0.1, 2.1, 4.1, 6.1$

In Fig.4, the concentration of cancer cells ( $u_2$ ) at the secondary site initially has a value of zero, then it begins to increase closer to zero until ( $t = 20$ ) due to the effect of time delay ( $\tau$ ) then the curve starts to rise quickly.

The study also see that no matter how different the values of ( $\alpha_1$ ) are, the concentration of cancer cells in the secondary site ( $u_2$ ) equals 2300 after ( $t = 26$ ) and is stable there.

The cancer cells ( $u_2$ ) have faster growth when the birth rate ( $\alpha_1$ ) is lower.

### CONCLUSION

By numerically simulating the birth rate ( $\alpha_1$ ) of normal cells at the primary site using the parameters selected, it is assumed that the birth

rate ( $\alpha_2$ ) grows faster than normal cells ( $\alpha_1$ ), thus i.e., ( $0 < \alpha_1 < \alpha_2$ ).

The study obtained abnormal cells equilibrium point  $E = (0, \tilde{x}_2, 0, \tilde{u}_2) = (0, 2079, 0, 2300)$ .

The equilibrium point  $(0, \tilde{x}_2, 0, \tilde{u}_2)$  don't depend on  $\alpha_1$  to be stable.

There is a small effect observed that smaller values of birth rate ( $\alpha_1$ ) are associated with the faster growth of cancer cells in the two sites.

Minimum values of birth rate ( $\alpha_1$ ) are associated with rapid death of normal cells at both sites.

The results obtained from determining stable equilibrium points and those obtained from numerical simulation are compatible.

### THE PROGRAM OF MATLAB

```
function sol = Change_alpha_1
clear; clc; close all
% This code to solve the No treatment
case for
% different change birth rate alpha_1
with time delay:
% dx1/dt = alpha_1*x1*(1-(x1/K1)) -
q_1*x1*x2,
% dx2/dt = alpha_2*x2*(1-(x2/K2)) -
q_2*x1*x2 - delta*x2,
% du1/dt = beta_1*u1*(1-(u1/L1)) -
r_1*u1*u2,
% du2/dt = beta_2*u2*(1-(u2/L2)) -
r_2*u1*u2
% + eipson*delta*x2(t-tau),
% with the following parameters and
initial conditions.
tau =20;
alpha_1 = 0.1:2:6.1;
x1_0 =1460;x2_0 = 0.01; u1_0 = 1750;
u2_0 = 0;
%-----
for i = 1:4
```

```
Alpha_1 = alpha_1 (i);
options = ddeset('RelTol', 1e-9,
'AbsTol', 1e-5,...
'InitialY',[x1_0;x2_0 ; u1_0;
u2_0] );
sol(i) =
dde23(@change_alpha_1,tau,[x1_0;x2_0 ;
u1_0; u2_0],...
[0,30],options,Alpha_1);
end
%-----
figure
plot (sol(1).x,
sol(1).y(1,:),sol(2).x,
sol(2).y(1,:),...
sol(3).x, sol(3).y(1,:),sol(4).x,
sol(4).y(1,:), ...
'linewidth', 2), hold on, grid on
xlabel('Time (t)
','FontName','Times','FontSize',16),
ylabel('Normal cells (X_1) at primary
site','FontName',...
'Times','FontSize',16)
legend ('\alpha_1 = 0.1'
,'\alpha_1 = 2.1','\alpha_1 =
4.1'...
,'\alpha_1 = 6.1')
%-----
figure
plot (sol(1).x,
sol(1).y(2,:),sol(2).x,
sol(2).y(2,:),...
sol(3).x, sol(3).y(2,:),sol(4).x,
sol(4).y(2,:), ...
'linewidth', 2), hold on, grid on
xlabel('Time (t)
','FontName','Times','FontSize',16),
ylabel('Cancer cells (X_2) at primary
site','FontName',...
'Times','FontSize',16)
legend ('\alpha_1 = 0.1'
,'\alpha_1 = 2.1','\alpha_1 =
4.1'...
,'\alpha_1 = 6.1')
%-----
figure
plot (sol(1).x,
sol(1).y(3,:),sol(2).x,
sol(2).y(3,:),...
sol(3).x, sol(3).y(3,:),sol(4).x,
sol(4).y(3,:), ...
'linewidth', 2), hold on, grid on
xlabel('Time (t)
','FontName','Times','FontSize',16),
ylabel('Normal cells (U_1) at
secondary site','FontName',...
```

```

    'Times','FontSize',16)
legend ('\alpha_1 = 0.1'
, '\alpha_1 = 2.1', '\alpha_1 =
4.1'...
, '\alpha_1 = 6.1')
%-----
figure
plot (sol(1).x,
sol(1).y(4,:),sol(2).x,
sol(2).y(4,:),...
sol(3).x, sol(3).y(4,:),sol(4).x,
sol(4).y(4,:), ...
'linewidth', 2), hold on, grid on
xlabel('Time (t)
','FontName','Times','FontSize',16),
ylabel('Cancer cells (U_2) at
secondary site','FontName',...
'Times','FontSize',16)
legend ('\alpha_1 = 0.1'
, '\alpha_1 = 2.1', '\alpha_1 =
4.1'...
, '\alpha_1 = 6.1')
%-----
function dw = change_alpha_1
(t,w,Z,Alpha_1)
%alpha_1 = 1.5;
alpha_2 = 10;
K1 = 1460;
K2 = 2100;
L1 = 1750; L2 = 2300;
q_1 = 0.0075; q_2 = 0.005;
r_1 = 0.002; r_2 = 0.001;
beta_1 = 2; beta_2 = 12;
delta = 0.1; epsilon = 0.0001;

dw = zeros (4,1);
x1 = w(1);
x2 = w(2);
u1 = w(3);
u2 = w(4);

if isempty(Z)
dw(1) = Alpha_1*x1*(1-(x1/K1)) -
q_1*x1*x2;
dw(2) = alpha_2*x2*(1-(x2/K2)) -
q_2*x1*x2 - delta*x2;
dw(3) = beta_1*u1*(1-(u1/L1)) -
r_1*u1*u2;
dw(4) = beta_2*u2*(1-(u2/L2)) -
r_2*u1*u2 + (epsilon*delta*x2);
else
ylag = Z(2);
dw(1) = Alpha_1*x1*(1-(x1/K1)) -
q_1*x1*x2;
dw(2) = alpha_2*x2*(1-(x2/K2)) -
q_2*x1*x2 - delta*x2;

```

```

dw(3) = beta_1*u1*(1-(u1/L1)) -
r_1*u1*u2;
dw(4) = beta_2*y1ag*(1-(u2/L2)) -
r_2*u1*u2 + (epsilon*delta*u2);
end

```

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### المخلص

النموذج الذي يتألف من أربعة معادلات تفاضلية غير خطية يوصف الانتشار غير المُعالج للسرطان من موقع أساسي إلى موقع ثانوي. يأخذ النموذج في الاعتبار المنافسة - التي قد تكون مؤجلة - بين الخلايا السليمة والخلايا الخبيثة على الموارد في كلا الموقعين. كما يتضمن مجموعة من معدلات ولادة الخلايا الطبيعية المختلفة ضمن نطاق متناسب. في هذه الدراسة، تم حساب نقاط التوازن للنموذج عددياً، وتم تقييم استقرارها. ومن خلال محاكاة سلوك الخلايا بمرور الوقت، يتم استخدام نهج Runge-Kutta لدراسة كيفية تأثير التغيرات في معدل الولادة على النموذج. وقد تم في دراستنا تحليل تأثير تغيير معدل الولادة على ديناميكيات الخلايا من خلال مقارنة النتائج المستخرجة من الرسوم البيانية.

**الكلمات المفتاحية:** نموذج لمرض السرطان، معدل الولادة، رونج كوتا، التحليل الرياضي.

