A population model of two-strains tumors with piecewise constant arguments

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ABSTRACT

In this study, the population growth of the brain tumor GBM, is constructed such as

\[
\begin{align*}
\frac{dx}{dt} &= px(t) + r_1 x(t)\left(R_1 - \alpha_1 x(t) - \alpha_2 x(\lfloor t \rfloor)\right) - \gamma_1 x(t) y(\lfloor t \rfloor) - d_1 x(t) x(\lfloor t \rfloor) \\
\frac{dy}{dt} &= r_2 y(t)\left(R_2 - \beta_1 y(t) - \beta_2 y(\lfloor t \rfloor)\right) + \gamma_1 x(\lfloor t \rfloor) y(t) - d_2 y(t) y(\lfloor t \rfloor)
\end{align*}
\]

where \( t = 0 \), the parameters \( \alpha_1, \alpha_2, \beta_1, \beta_2, \gamma_1, p, d_1, d_2, R_1, R_2, r_1 \) and \( r_2 \) are positive real numbers and \( \lfloor t \rfloor \) denotes the integer part of \( t \in [0,8) \). System (A) explains a tumor growth, that produces after a specific time another tumor population with different growth rate and different treatment susceptibilities. The local and global stability of this model is analyzed by using the theory of differential and difference equations. Simulations and data of GBM give a detailed description of system (A) at the end of the paper.

Keywords: Differential equation; difference equations; local stability; global stability; boundedness

INTRODUCTION

Glioblastoma multiforme is the most aggressive of the gliomas, a collection of tumors arising from glia or their precursors within the central nervous system. Most patients with GBMs die of their disease in less than a year and essentially none has long-term survival, Holland (2000). In the first stage of GBM, the tumor has a monoclonal origin, which changes after reaching a specific density. This kind of tumor can develop multiple sub-population with different growth rates and treatments susceptibilities. For this, during the treatment process a formidable obstacle can be obtained. Various papers about the characteristic behavior of GBM or tumor population with multiform are written, where some of them are Berkmann et al. (1992); Coons & Johnson (1993); Paulus & Peiffer (1989); Yung et al. (1982). Brain tumors are ideal candidates for theoretical modeling. Mathematical approaches to tumor treatment offer a perspective
that current in vivo/in vitro techniques cannot, Coldman & Goldie (1979); Panetta (1998).

By describing the tumor phenomena the best known modeling is the Gompertz’s model,

\[ V = V_0 \exp \left( \frac{A \cdot \left(1 - \exp(-Bt)\right)}{B} \right) \]

(1.1)

where \( V \) describes the volume of the tumor, \( t \) denotes the time, \( V_0 \) is the volume at time \( t=0 \), \( A \) and \( B \) are parameters that have to be specified, Birkhead (1987).

Coldman & Goldie (1979) proposed a model, which links a Tumor’s drug sensitivity to its rate of spontaneous resistance mutations such as

\[ \frac{d\mu}{dt} = \frac{\mu}{N} + \alpha \left(1 - \frac{\mu}{N}\right) \]

(1.2)

where \( \mu \) is the mean volume of the resistant strain and \( N \) the total volume of the tumor. The parameter \( \alpha \) is the mutation rate per cell generation.

Panetta (1998) modeled the size of two sub-populations in time such as

\[
\begin{cases}
\frac{dx}{dt} = (r_1 - d_1(t))x \\
\frac{dy}{dt} = b_1 d_1(t)x + (r_2 - d_2(t))y
\end{cases}
\]

(1.3)

where \( x \) represents the sensitive cell population, \( y \) the resistant cell population, \( r_1 \) and \( r_2 \) are the growth rates, \( d_1 \) and \( d_2 \) are their drug sensitivities, respectively.

Birkhead et al. (1987), have considered both cycling and resting tumor cells in their study. The difference between the two models is that sensitive cells could convert to resistant cells, while cycling and resting cells could inter-convert. Similar works about modeling tumor behaviors can be found in Schmitz et al. (2002); De Vlader & Gonzalez (2004); Gevertz & Toquato (2006); Mansury et al. (2006).

In some biological situations Mathematical approximation for population growth involves nonlinear differential equations, May (1975); May & Oester (1976). It is generally known that for an overlapping generation of a single species, a model with a differential equation is preferred. If there is a non-overlapping generation of single species, then it is convenient to construct a model with a difference equation, Allen (2007); Hoppenstead (2004); Rubinow (2002). For both time situations, continuous and discrete, there is some population dynamics in ecosystem, which combine the properties of both differential and difference equations, where the use of piecewise constant arguments come into question. For such biological events it may be suitable to construct a model with piecewise constant arguments, see Cooke & Huang (1991); Gopalsamy & Liu (1998); Gurcan & Bozkurt (2009); Liu & Gopalsamy (1999); Ozturk & Bozkurt (2011).
According to Gopalsamy & Liu (1998), the differential equation
\[
\frac{dN(t)}{dt} = rN(t)\left(1 - aN(t) - bN\left([t]\right)\right)
\]

(1.4)

was considered, where \(N(t)\) denotes the biomass (or population density) of a single species, \(r\), \(a\), \(b\) and \(t\) are positive numbers. Using the Lyapunov function, they proved sufficient condition for all positive solutions of equation (1.4). A general differential equation of (1.4) can be shown in Liu & Gopalsamy, (1999), were by using the lemma of Cooke and Huang, see Cooke & Huang (1991) the global attractivity of the positive equilibrium point are proven.

Gurcan & Bozkurt (2009), considered the logistic equation
\[
\frac{dx}{dt} = r x(t)\left(1 - ax(t) - \beta_0 x\left([t]\right)\right) - \beta_1 x\left([t-1]\right)),
\]

(1.5)

where \(t \geq 0\) and the parameters \(\alpha\), \(\beta_0\), \(\beta_1\) and \(r\) denote positive numbers. The local asymptotic stability of the positive equilibrium point of equation (1.5) was proven by using the Linearized Stability Theorem and the global asymptotic stability by using a suitable Lyapunov function. A general differential equation (1.5) was shown in Ozturk & Bozkurt (2011), where additionally a detailed description and condition of semicycle and damped oscillation of the positive solutions are proved.

In this paper, the growth of GBM has been considered. This tumor has two sub-populations, the sensitive cells and the resistant cells, where the model is constructed such as
\[
\begin{align*}
\frac{dx}{dt} &= p x(t) + r x(t)\left(R_1 - \alpha_1 x(t) - \alpha_2 x\left([t]\right)\right) - \gamma_1 x(t) y\left([t]\right) - d_1 x(t) x\left([t]\right) \\
\frac{dy}{dt} &= r_2 y(t)\left(R_2 - \beta_1 y(t) - \beta_2 y\left([t]\right)\right) + \gamma_1 x\left([t]\right) y(t) - d_2 y(t) y\left([t]\right)).
\end{align*}
\]

(1.6)

Here, \(t \geq 0\) and the parameters \(\alpha_1\), \(\alpha_2\), \(\beta_1\), \(\beta_2\), \(\gamma_1\), \(p\), \(d_1\), \(d_2\), \(r_1\) and \(r_2\) denote positive numbers. \(p\) is the division rate of the sensitive cells and the parameter \(\alpha_1\), \(\alpha_2\), \(\beta_1\) and \(\beta_2\) are necessary parameters for the logistic differential equations of the tumor populations. \(\gamma_1\) is the converting rate of sensitive cells to resistant cells. The parameters \(d_1\) and \(d_2\) are their dead rate caused from drugs, respectively. In section 2, we investigate the local and global behavior of the nonlinear difference solutions of (1.6) based on specific conditions. Furthermore, the boundedness nature of the positive solutions of (1.6) was considered. Simulations and the data of GBM give a detailed description of the behavior of system (1.6) at the end of the paper.
LOCAL STABILITY AND GLOBAL ASYMPTOTIC STABILITY

On an interval of the form \( t \in [n, n+1] \), one can write (6) as

\[
\begin{align*}
\frac{dx}{dt} &= \left\{ p + r_1 R_1 - (\alpha_2 r_1 + d_1)x(n) - \gamma_1 y(n) \right\}x(t) = -\alpha_1 r_1(x(t))^2 \\
\frac{dy}{dt} &= \left\{ r_2 R_2 - (\beta_2 r_2 + d_2)y(n) + \gamma_1 x(n) \right\}y(t) = -\beta_1 r_2(y(t))^2,
\end{align*}
\]

(2.1)

where for \( n = 0, 1, 2 \), and \( t \to n+1 \) the solution is

\[
\begin{align*}
x(n+1) &= \frac{x(n)\{p + r_1 R_1 - (\alpha_2 r_1 + d_1)x(n) - \gamma_1 y(n)\}}{\{p + r_1 R_1 - (\alpha_2 r_1 + d_1)x(n) - \gamma_1 y(n)\}\exp\left(-\{p + r_1 R_1 - (\alpha_2 r_1 + d_1)x(n) - \gamma_1 y(n)\}\right) + \alpha_1 r_1 x(n)} \\
y(n+1) &= \frac{y(n)\{r_2 R_2 - (\beta_2 r_2 + d_2)y(n) + \gamma_1 x(n)\}}{\{r_2 R_2 - (\beta_2 r_2 + d_2)y(n) + \gamma_1 x(n)\}\exp\left(-\{r_2 R_2 - (\beta_2 r_2 + d_2)y(n) + \gamma_1 x(n)\}\right) + \beta_1 r_2 y(n)}.
\end{align*}
\]

(2.2)

In the following, we assume that

\[
p + r_1 R_1 - (\alpha_2 r_1 + d_1)x(n) - \gamma_1 y(n) \neq 0
\]

(2.3)

and

\[
r_2 R_2 - (\beta_2 r_2 + d_2)y(n) + \gamma_1 x(n) \neq 0.
\]

(2.4)

To investigate more about the behavior of (1.6) we continue the analysis, since (2.2) is a system of difference equations. First, we need to obtain the positive equilibrium point of (2.2), which is also the critical points of (1.6). Computations reveal that the positive equilibrium points of (8) is

\[
\mu = (\bar{x}, \bar{y}) = \left( \frac{(p + r_1 R_1)\{d_2 + \beta_1 r_2 + \beta_2 r_2\} - r_1 R_2 \gamma_1}{d_1 + \alpha_2 r_1 + \alpha_1 r_1} \right) + \left( p + r_1 R_1 \right) \gamma_1 \\
\]

(2.5)

where

\[
\gamma_1 < \frac{(p + r_1 R_1)\{d_2 + \beta_1 r_2 + \beta_2 r_2\}}{r_2 R_2}
\]

(2.6)

and

\[
\begin{align*}
A &= p + r_1 R_1 - (\alpha_2 r_1 + d_1)\bar{x} - \gamma_1 \bar{y} = \frac{\alpha_1 r_1 (p + r_1 R_1)\{d_2 + \beta_1 r_2 + \beta_2 r_2\} - \alpha_1 r_1 R_2 \gamma_1}{d_1 + \alpha_2 r_1 + \alpha_1 r_1} > 0 \\
B &= r_2 R_2 - (\beta_2 r_2 + d_2)\bar{y} + \gamma_1 \bar{x} = \frac{\beta_1 R_2 \gamma_1^2 \{d_1 + \alpha_2 r_1 + \alpha_1 r_1\} + (p + r_1 R_1) \gamma_1 \beta_1 r_2}{d_1 + \alpha_2 r_1 + \alpha_1 r_1} > 0
\end{align*}
\]

(2.7)

Linearizing system (2.2) about the positive equilibrium point, we obtain for \( n = 0, 1, 2, \ldots \) the associated characteristic equation of (2.2) as
\[ \lambda^2 - (a_{11} + a_{22}) \lambda + (a_{11}a_{22} - a_{12}a_{21}) = 0, \] (2.7)

where

\[
\begin{align*}
    a_{11} &= (d_1 + \alpha_2 r_1 + \alpha_1 r_1) e^{-A} - (d_1 + \alpha_2 r_1) \
    a_{12} &= \frac{\gamma_1 (e^{-A} - 1)}{\alpha_1 r_1} \
    a_{21} &= \frac{\gamma_1 (1 - e^{-B})}{\beta_1 r_2} \
    a_{22} &= \frac{(d_2 + \beta_2 r_2 + \beta_1 r_2) e^{-B} - (d_2 + \beta_2 r_2)}{\beta_1 r_2}.
\end{align*}
\] (2.8)

**Theorem 2.1.** Let \( \alpha_2 > \alpha_1 \) and \( r_1 r_2 > \frac{2(\gamma_1)^2}{\alpha_1 \beta_1} \). If

\[
\ln\left(\frac{d_1 + \alpha_2 r_1 + \alpha_1 r_1}{d_1 + \alpha_2 r_1}\right) < A < \ln\left(\frac{d_1 + \alpha_2 r_1 + \alpha_1 r_1}{d_1 + \alpha_2 r_1 - \alpha_1 r_1}\right)
\] (2.9)

and

\[
B < \ln\left(\frac{d_2 + \beta_2 r_2 + \beta_1 r_2}{d_2 + \beta_2 r_2}\right),
\] (2.10)

then the positive equilibrium point of system (8) is locally asymptotically stable.

**Proof.** By the Linearized Stability Theorem, see Gibbons et al. (2002), the positive equilibrium point of (8) is locally asymptotically stable if and only if

\[
|a_{11} + a_{22}| < 1 + a_{11}a_{22} - a_{12}a_{21} < 2
\] (2.11)

holds. From condition (17), we can write

\[
\left( (d_1 + \alpha_2 r_1 + \alpha_1 r_1) e^{-A} - (d_1 + \alpha_2 r_1) \right) \cdot \left( (d_2 + \beta_2 r_2 + \beta_1 r_2) e^{-B} - (d_2 + \beta_2 r_2) \right) < \alpha_1 \beta_1 r_1 r_2 - (\gamma_1)^2 \cdot (1 - e^{-A}) (1 - e^{-B})
\] (2.12)

Since \( A > 0 \) and \( B > 0 \), if

\[
A > \ln\left(\frac{d_1 + \alpha_2 r_1 + \alpha_1 r_1}{d_1 + \alpha_2 r_1}\right)
\] (2.13)
and
\[ B < \ln\left( \frac{d_2 + \beta_2 r_2 + \beta r_2}{d_2 + \beta_2 r_2} \right), \] (2.14)
then we have
\[ (d_2 + \beta_2 r_2 + \beta_1 r_2)e^{-B} - (d_2 + \beta_2 r_2) > 0 \] (2.15)
and
\[ (d_1 + \alpha_2 r_1 + \alpha_1 r_1)e^{-A} - (d_1 + \alpha_2 r_1) < 0. \] (2.16)
Additionally, we can write
\[ \alpha_1 \beta_1 r_1 r_2 - (\gamma_1)^2 + (\gamma_1)^2 \left( e^{-A} + e^{-B} \right) > (\gamma_1)^2 e^{-(A+B)}, \] (2.17)
since
\[ e^{(A+B)} > 1 = \frac{(\gamma_1)^2}{\alpha_1 \beta_1 r_1 r_2 - (\gamma_1)^2} \] (2.18)
and
\[ r_1 r_2 > \frac{2(\gamma_1)^2}{\alpha_1 \beta_1} > \frac{(\gamma_1)^2}{\alpha_1 \beta_1}. \] (2.19)

From (2.13)-(2.19), the conditions to hold the second part of the inequality in (2.11) are obtained. Furthermore, to consider the inequalities for the left side of (2.11), the following ones have to be considered;

(i) \[ \beta_1 r_2 \left( (d_1 + \alpha_2 r_1 + \alpha_1 r_1)e^{-A} - (d_1 + \alpha_2 r_1) \right) + \alpha_1 r_1 \left( (d_2 + \beta_2 r_2 + \beta r_2)e^{-B} - (d_2 + \beta_2 r_2) \right) < \alpha_1 \beta_1 r_1 r_2 + \left( (d_1 + \alpha_2 r_1 + \alpha_1 r_1)e^{-A} - (d_1 + \alpha_2 r_1) \right) \]
\[ \cdot \left( (d_2 + \beta_2 r_2 + \beta_1 r_2)e^{-B} - (d_2 + \beta_2 r_2) \right) + (\gamma_1)^2 \cdot \left( 1 - e^{-A} \right) \left( 1 - e^{-B} \right) \]

(ii) \[- \alpha_1 \beta_1 r_1 r_2 - \left( (d_1 + \alpha_2 r_1 + \alpha_1 r_1)e^{-A} - (d_1 + \alpha_2 r_1) \right) \]
\[ \cdot \left( (d_2 + \beta_2 r_2 + \beta_1 r_2)e^{-B} - (d_2 + \beta_2 r_2) \right) - (\gamma_1)^2 \cdot \left( 1 - e^{-A} \right) \left( 1 - e^{-B} \right) \]
\[ < \beta_1 r_2 \left( (d_1 + \alpha_2 r_1 + \alpha_1 r_1)e^{-A} - (d_1 + \alpha_2 r_1) \right) + \alpha_1 r_1 \left( (d_2 + \beta_2 r_2 + \beta_1 r_2)e^{-B} - (d_2 + \beta_2 r_2) \right), \]

By considering these, we obtain
\[ \left( (d_1 + \alpha_2 r_1) - (d_1 + \alpha_2 r_1 + \alpha_1 r_1)e^{-A} \right) \cdot \left( (d_2 + \beta_2 r_2 + \beta_1 r_2)e^{-B} - (d_2 + \beta_2 r_2) \right) < \beta_1 r_2 \left( (d_1 + \alpha_2 r_1 + \alpha_1 r_1)e^{-A} - (d_1 + \alpha_2 r_1) \right). \] (2.20)
since $A > 0$. Furthermore, from
\[ \alpha_1 r_1 \left( (d_2 + \beta_2 r_2 + \beta_1 r_1) e^{-B} - (d_2 + \beta_2 r_2) \right) < \alpha_1 \beta_1 r_1 r_2, \quad (2.21) \]
we have $e^{-B} < 1$, which is always true, since $B > 0$.

From (ii), if
\[
\left( (d_1 + \alpha_2 r_1) - (d_1 + \alpha_2 r_1 + \alpha_1 r_1) e^{-A} \right) \left( (d_2 + \beta_2 r_2 + \beta_1 r_1) e^{-B} - (d_2 + \beta_2 r_2) \right) < \alpha_1 r_1 \left( (d_2 + \beta_2 r_2 + \beta_1 r_1) e^{-B} - (d_2 + \beta_2 r_2) \right),
\quad (2.22) \]
for $\alpha_2 > \alpha_1$, we get
\[ A < \ln \left( \frac{d_1 + \alpha_2 r_1 + \alpha_1 r_1}{d_1 + \alpha_2 r_1 - \alpha_1 r_1} \right). \quad (2.23) \]

Considering both (2.13) and (2.23), the inequality (2.9) is obtained. In addition, from the inequality
\[ \beta_1 r_1 \left( (d_1 + \alpha_2 r_1) - (d_1 + \alpha_2 r_1 + \alpha_1 r_1) e^{-A} \right) < \alpha_1 \beta_1 r_1 r_2, \quad (2.24) \]
we get (2.23), which completes our proof.

**Theorem 2.2.** Suppose that the conditions in Theorem 2.1 hold. Furthermore, assume that
\[ \alpha_1 r_1 x(n) < p + r_1 R_1 - (\alpha_2 r_1 + d_1) x(n) - \gamma_1 y(n) < \ln \left( \frac{2x - x(n)}{x(n)} \right) \quad (2.25) \]
and
\[ \beta_1 r_2 < r_2 R_2 + \gamma_1 x(n) - (\beta_2 r_2 + d_2) y(n) < \ln \left( \frac{2y - y(n)}{y(n)} \right). \quad (2.26) \]

For $n = 0, 1, 2, \ldots$, if
\[ x(n) < 2\bar{x} \text{ and } y(n) < 2\bar{y} \quad (2.27) \]
then the positive equilibrium point of system (8) is globally asymptotically stable.

**Proof.** We consider a Lyapunov function $V(n)$ defined by
\[ V(n) = (V_1(n), V_2(n)) = \left\{ X(n) - \mu \right\}^2, \quad (2.28) \]
where $n = 0, 1, 2$, and $X(n) = (x(n), y(n))$. From the change along the solutions of (32), we obtain
\[ \Delta V_1(n) = \left\{ x(n+1) - x(n) \right\} \left\{ x(n+1) + x(n) - 2\bar{x} \right\} \quad (2.29) \]
and
\[ \Delta V_2(n) = \left\{ y(n+1) - y(n) \right\} \left\{ y(n+1) + y(n) - 2\bar{y} \right\}. \quad (2.30) \]
By using (2.25), one can obtain
\[ x(n+1) - x(n) > 0. \] (2.31)

Furthermore if (2.27) holds for \( x(n) \), then it is easy to obtain the following one;
\[ x(n+1) + x(n) - 2x = A \left( x(n) + \left( x(n) - 2\bar{x} \right) e^{-\alpha A} \right) + \alpha_1 r_1 x(n) \left( 1 - e^{-\alpha A} \right) \left( x(n) - 2\bar{x} \right) < 0. \] (2.32)

From (2.25) and (2.27), we get in this case \( \Delta V_1(n) < 0. \) In similar way, for the condition (2.26), we have
\[ y(n+1) - y(n) > 0 \quad \text{and} \quad y(n+1) + y(n) - 2\bar{y} < 0, \] (2.33)
where, \( y(n) < 2\bar{y} \). This implies that \( \Delta V_1(n) < 0. \) which completes the proof of global asymptotic stability.

**Theorem 2.3** Let \( \{ x(n), y(n) \}_{n=0}^{\infty} \) be a positive solution of (2.2). Assume that for \( n=0, 1 \), the conditions
\[ \alpha_1 r_1 x(n) < p + r_1 R_1 - \left( \alpha_2 r_1 + d_1 \right) x(n) - \gamma_1 y(n) \] (2.34)
and
\[ \beta_1 r_2 y(n) < r_2 R_2 + y(n) - \left( \beta_2 r_2 + d_2 \right) y(n) \] (2.35)
hold. Then all positive solutions of (2.2) are in the interval
\[ x(n) \in \left( 0, \frac{p + r_1 R_1}{\alpha_1 r_1} \right) \quad \text{and} \quad y(n) \in \left( 0, \frac{\alpha_1 R_2 r_2 + \alpha_2 \gamma_1 \left( p + r_1 R_1 \right)}{\alpha_1 \beta_1 r_2} \right). \] (2.36)

**Proof.** Let \( \alpha_1 r_1 x(n) < p + r_1 R_1 - \left( \alpha_2 r_1 + d_1 \right) x(n) - \gamma_1 y(n) \). Then we can write
\[ p + r_1 R_1 - \left( \alpha_2 r_1 + d_1 \right) x(n) - \gamma_1 y(n) < p + r_1 R_1 \] (2.37)
and from
\[ -(p + r_1 R_1 - \left( \alpha_2 r_1 + d_1 \right) x(n) - \gamma_1 y(n)) > -(p + r_1 R_1), \] (2.38)
we have
\[ e^{-\left( p + r_1 R_1 - \left( \alpha_2 r_1 + d_1 \right) x(n) - \gamma_1 y(n) \right)} > e^{-\left( p + r_1 R_1 \right)}. \] (2.39)

By using both (2.37) and (2.39), the first equation of (2.2) satisfy
\[ x(n+1) < \frac{x(n) \left( p + r_1 R_1 \right)}{\left( p + r_1 R_1 - \left( \alpha_2 r_1 + d_1 \right) x(n) - \gamma_1 y(n) \right) e^{-\left( p + r_1 R_1 \right)} + \alpha_1 r_1 x(n) \left( 1 - e^{-\left( p + r_1 R_1 \right)} \right)}, \] (2.40)
Furthermore, since \( \alpha_1 r_1 x(n) < p + r_1 R_1 - (\alpha_2 r_1 + d_1) x(n) - \gamma_1 y(n) \), we can write
\[
\frac{1}{p + r_1 R_1 - (\alpha_2 r_1 + d_1) x(n) - \gamma_1 y(n)} < \frac{1}{\alpha_1 r_1 x(n)}. \tag{2.41}
\]

Using (2.41) in (2.40), we get
\[
x(n + 1) < \frac{x(n)(p + r_1 R_1)}{\alpha_1 r_1 x(n)e^{-(p+r_1 R_1)} + \alpha_1 r_1 x(n)(1 - e^{-(p+r_1 R_1)})} = \frac{p + r_1 R_1}{\alpha_1 r_1}. \tag{2.42}
\]

In addition, since \( \beta_2 r_2 y(n) < r_2 R_2 + \gamma_1 x(n) - (\beta_2 r_2 + d_2) y(n) \), we obtain
\[
r_2 R_2 + \gamma_1 x(n) - (\beta_2 r_2 + d_2) y(n) < r_2 R_2 + \gamma_1 x(n) \tag{2.43}
\]
and
\[
\frac{1}{r_2 R_2 + \gamma_1 x(n) - (\beta_2 r_2 + d_2) y(n)} < \frac{1}{\beta_2 r_2 y(n)}. \tag{2.44}
\]

Considering both (2.43) and (2.44), we get
\[
y(n + 1) < \frac{r_2 R_2 + \gamma_1 x(n)}{\beta_2 r_2} < \frac{\alpha_1 R_2 r_2 + \gamma_1 (p + r_1 R_1)}{\alpha_1 \beta_2 r_1 r_2}, \tag{2.45}
\]
which completes the proof.

**Example:** The values of the parameters of (2.2) are chosen as given in Schmitz et al. (2002) and in view the obtained results. The table is given as follows;

| **Table 1. Values of the parameter of system (2.1)** |
|---------------------------------|-----------------|
| Parameter                       | Value           |
| \( p \)                         | 0.192           |
| \( K_1 \)                       | 0.42 * 38^{2/3} = 4.704 |
| \( K_2 \)                       | 0.11 * 38^{2/3} = 1.232 |
| \( \Gamma \)                    | \( \gamma \in [10^{-5}, 10^{-2}] \) |
| \( \alpha_i \)                  | \( \alpha_i \in [0.5, 0.95] \) |
| \( \beta_i \)                   | \( \beta_i \in [0.05, 0.2] \) |
| \( d_1 \)                       | 0.001           |
| \( d_2 \)                       | 0.00001         |
We want to consider the behaviors for the converting rates $\gamma_1 = 0.01$ and $\gamma_1 = 0.00001$. Both populations have different growth rates. In this example, we have constructed a relation between both population such as $r = r_1$ and $(1.05)r = r_2$. The initial conditions are $x(0)=0.82$ and $y(0)=0.23$, where the x-axis of the graph denotes the growth rate of the population and the y-axis the per capita growth of both population. The blue and the red graph symbolize the sensitive cells population ($x(n)$) and the resistant cells population ($y(n)$), respectively. Figure 1 show the behavior of the sensitive cells and resistant cells, where the mutation rate is $\gamma_1 = 0.01$. Here, it is shown that at last the resistant cells will cover the sensitive cells, as also explained in Schmitz et al. (2002).

![Fig. 1 Figure for the coordinates ($r_1, x(n+1)/x(n)$) and ($r_2, y(n+1)/y(n)$), where $\gamma_1 = 0.01$](image)

Figure 2, show the behavior of the sensitive cells and resistant cells, where $\gamma_1 = 0.00001$. It is clear that during the initial phases, the volume of the sensitive cells are more than the resistant cells. But since the population growth rate of the resistant cells is greater than the sensitive cells, after a specific time the resistant cells will occur on the wall of the sensitive tumor cells, see also Schmitz et al. (2002).
A population model of two-strains tumors with piecewise constant arguments

Fig. 2. Figure for the coordinates \((r_1, x(n+1)/x(n))\) and \((r_2, y(n+1)/y(n))\), where \(\gamma_1 = 0.00001\).

NUMERICAL RESULTS AND COMMENTS

In section 2, the local and global asymptotic stability of the positive equilibrium point of system (8) have been analyzed in Theorem 2.1 and Theorem 2.2, respectively. Theorem 2.3 was an important proof to show the bound of both tumor structures. The parameters are used from the data of Schmitz, et al. (2002), where it has been shown that a sensitive tumor population with the mutation rate \(\gamma_1 = 0.00001\), occur on the wall of the sensitive cells after a specific density and specific time. Furthermore, if the mutation rate is \(\gamma_1 = 0.01\), then the resistant tumor population will cover the sensitive tumor cells, which makes the treatment process more difficult than the phenomena shown in Figure 1.

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خلاصة

نبني في هذه الدراسة نموذجاً رياضياً لمجتمع إحصائي للنمو السرطاني لأورام الدماغ. يقوم النموذج الذي وصفنا بإيضاح النمو للأورام ثم يقوم بعد زمن محدد بإنتاج مجتمع إحصائي جديد له معدل نمو مختلف وله قابلية علاج مختلفة. نقوم بتحليل الاستقرار المحلي والاستقرار الشامل لهذا النموذج وذلك باستخدام نظرية المعادلات التفاضلية والمعادلات الفرقة. وتقدم المعطيات والمحاكاة وصفاً تفصيلياً للنموذج المبني على نظامنا وذلك في نهاية البحث.